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THE REACTION OF STANNIC CHLORIDE AND BROMIDE WITH AMINO ACIDS

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We have previously [1] studied the complex-forming reactions of $SnCl_4$ and $SnBr_4$ with glycine in acetic and trichloroacetic acids. In these studies it was established that when halides of tetravalent tin act on a solution of glycine in acetic acid, the complex compounds $SnX_4 \cdot 2AcH \cdot 2GlH$ and $SnX_4 \cdot 4GlH$ are formed, and when stannic chloride acts on a solution of glycine in CCl_3COOH, the compound $SnX_4 \cdot 2GlH$ is formed.

Continuing the investigation in this direction, we decided to study the reaction of stannic chloride and bromide with α- and β-alanine, and also with leucine in different solvents (CH_3COOH, CCl_3COOH, and CH_3NO_2).

EXPERIMENTAL

Benzene, acetic and trichloroacetic acids, and also stannic chloride and bromide were purified in the manner previously described [1, 2]; the nitromethane was dried over P_2O_5 and then distilled twice; for the work we used the fraction that boiled at 98° (693 mm). The glycine, α- and β-alanine, and leucine of chemically pure grade were not purified further. The complex compounds of the stannic halides with the amino acids were prepared by carefully adding solutions of the amino acids in CH_3COOH (or CCl_3COOH or CH_3NO_2) to the stannic chloride or bromide at the calculated rate of 1 mole of stannic halide to 1, 2, or 4 moles of the amino acid. We prepared some complex compounds by displacement of the carboxylic acids from their salts with the amino acids by the stannic halides or by displacement of the carboxylic acids by amino acids from the appropriate complex compounds, and also by mixing the components in the determined stoichiometric ratio in the absence of a solvent. In cases where crystallization of the compounds occurred in the solvents, the crystals were separated from the mother liquors on glass filters, carefully washed with benzene, dried in a vacuum desiccator over P_2O_5, and then analyzed for tin and chlorine. In those cases where a viscous liquid separated out from the solutions, this liquid was separated from the mother liquor, washed with benzene or acetic acid, and placed in a vacuum desiccator to remove the solvent. Upon removal of the solvent, the viscous liquid was analyzed for tin and chlorine.

The Systems $SnCl_4$–α-AnH and $SnBr_4$–α-AnH

In Table 1 the results are presented of analysis of the precipitates obtained by mixing the components in different stoichiometric proportions in acetic and in trichloroacetic acids, and also in nitromethane.

The data that we obtained (Table 1) indicate that when $SnCl_4$ and $SnBr_4$ are mixed with solutions of α-alanine in CH_3COOH, CCl_3COOH, and CH_3NO_2, a number of products are formed. Formation of the complex compounds $[SnX_6](\alpha\text{-}AnH_2)_2$ shows that in CH_3COOH, CCl_3COOH, and CH_3NO_2 solvolysis takes place, which in our opinion goes according to the following scheme, where B = CH_3COO^- or $CH_2NO_2^-$:

1) $2AnH + 2BH \rightleftarrows 2B^- + 2AnH_2^+$

2) $2B^- + SnX_4 \rightleftarrows [SnX_4(B)_2]^{--}$

3) $[SnX_4(B)_2]^{--} + SnX_4 \rightleftarrows [SnX_6]^{--} + SnX_2(B)_2$

4) $2AnH + 2SnX_4 + 2BH \rightleftarrows [SnX_6](AnH_2)_2 + SnX_2(B)_2$

TABLE 1

Ratio of SnX_4: α-AnH	Found (%) Sn	Found (%) Cl(Br)	Composition of compound	Calculated (%) Sn	Calculated (%) Cl(Br)	Solvent	Remarks
Stannic chloride – α-alanine							
1 : 1	24.21 24.33 23.86 23.61	41.07 40.49 41.79 40.21	$[SnCl_4](\alpha\text{-}AnH_2)_2$	23.20	41.58	CH_3COOH	Crystals
1 : 1	24.65 24.60	39.18 40.38	$[SnCl_4](\alpha\text{-}AnH_2)_2$	23.20	41.58	CH_3NO_2	Crystals
1 : 2	22.88 22.68	25.72 25.85	$SnCl_4 \cdot 2AcH \cdot 2\alpha\text{-}AnH$	21.24	25.38	CH_3COOH	Crystals
1 : 2	0.44	17.93	$(\alpha\text{-}AnH)_2 \cdot HCl$	—	16.52	CH_3COOH	Crystals
1 : 2	23.86 23.37 23.69 23.38 23.44	40.41 41.10 41.04 41.82 41.41 41.36 41.30	$[SnCl_4](\alpha\text{-}AnH_2)_2$	23.20	41.58	CCl_3COOH	Crystals
1 : 4	19.79 19.21 18.94 18.98	22.60 22.21 23.56 22.53 22.38	$SnCl_4 \cdot 4\alpha\text{-}AnH$	19.24	23.06	CH_3COOH	Viscous liquid
1 : 4	—	16.53	$(\alpha\text{-}AnH)_2 \cdot HCl$	—	16.52	CH_3COOH	Crystals
1 : 4	16.11 15.79 16.18 16.00 16.84 16.84 16.99 16.76	18.95 19.56 19.52 19.24 19.48	$SnCl_4 \cdot 2CCl_3COOH \cdot 2\alpha\text{-}AnH$	15.50	18.52		Action of stannic chloride on alanine trichloroacetate
Stannic bromide – α-alanine							
1 : 1	15.85 15.71 15.24 15.50 15.09 15.74 15.37	61.14 60.27 60.92 61.06 61.63 61.35	$[SnBr_4](\alpha\text{-}AnH_2)_2$	15.24	61.65	CH_3COOH	Viscous liquid
1 : 2	15.84 15.97 15.74 16.01 16.20	43.23 42.9 (illegible) 43.7 (illegible) 43.87 43.13 43.27 43.05	$SnBr_4 \cdot 2AcH \cdot 2\alpha\text{-}AnH$	16.12	43.39	CH_3COOH	
1 : 2	19.10 19.15 19.28 19.36 19.14	51.28 51.53 51.12 51.23	$SnBr_4 \cdot 2\alpha\text{-}AnH$	19.25	51.84		In absence of solvent
1 : 4	15.07 15.12 15.10 14.92 14.99	39.95 40.09 40.27 40.03 39.88	$SnBr_4 \cdot 4\alpha\text{-}AnH$	14.93	40.26	CH_3COOH	Viscous liquid

From this diagram it can be seen that as a result of the solvolysis the compounds $SnX_2(CH_3COO)_2$ and $SnX_2(CH_2NO_2)_2$ are formed. These compounds should be comparatively soluble in CH_3COOH (or CH_3NO_2) and be found in the filtrate. To verify this we analyzed the solid phase and the filtrate of the mixtures (1 mole $SnCl_4$ to 1 mole α-alanine in CH_3COOH and CH_3NO_2). It turned out that the atomic ratio Sn: X in the precipitates was 1 : 5.9 and 1 : 5.5, respectively, and in the filtrates was 1 : 2.4 and 1 : 2.9. Thus, the results of the analysis confirm the suggested scheme of solvolysis.

When solutions of α-alanine in CH_3COOH (or in CH_3NO_2) are mixed with $SnCl_4$ (or $SnBr_4$), the reaction may stop at the stage of the formation of the complex compounds $SnX_4 \cdot 2BH \cdot 2\alpha\text{-AnH}$ (in the case of mixing the components in the ratio 1 : 2) and $SnX_4 \cdot 4\alpha\text{-AnH}$ (when the components are mixed in the ratio 1 : 4). The complex compound $SnCl_4 \cdot 4\alpha\text{-AnH}$* was also obtained by displacement of CH_3COOH with alanine from the internal sphere of the complex compound $SnCl_4 \cdot 2AcH \cdot 2\alpha\text{-AnH}$. The compound $SnBr_4 \cdot 2\alpha\text{-AnH}$ was formed when the components were mixed in the ratio 1 : 2 in the absence of solvent. We have not yet succeeded in preparing the analogous compound for stannic chloride, since α-alanine does not dissolve in stannic chloride even at the boiling point of the latter. We also tried to prepare this compound by displacement of CCl_3COOH by stannic chloride from alanine trichloroacetate. In contrast to glycine, however, when stannic chloride acts on alanine trichloroacetate, apparently addition of the alanine trichloroacetate to the stannic chloride takes place, and not displacement of the CCl_3COOH from its salt. From the mother liquors of the 1 : 2 and 1 : 4 mixtures we isolated alanine hydrochloride, formed as a result of solvolysis:

$$SnCl_4 \cdot 4\alpha\text{-AnH} + 2CH_3COOH \rightleftarrows SnCl_2(CH_3COO)_2 + 2(\alpha\text{-AnH})_2 \cdot HCl$$

The high tin content and low chlorine content in some reaction products, contrary to the formulas, can be explained by the presence of the solvolysis product $SnX_2(B)_2$.

The Systems $SnCl_4$–β-AnH and $SnBr_4$–β-AnH

In Table 2 the results are given for the analysis of the reaction products obtained when $SnCl_4$ and $SnBr_4$ were mixed with solutions of β-alanine in CH_3COOH and CCl_3COOH.

The results of the analysis of the reaction products (Table 2) show that when $SnCl_4$ was mixed with a solution of β-alanine in CH_3COOH (in the ratios 1 : 1, 1 : 2, and 1 : 4), and also in CCl_3COOH, the compound $[SnCl_6] \cdot (\beta\text{-AnH}_2)_2$ was formed. An analogous compound was obtained by the action of stannic bromide on solutions of β-alanine in CH_3COOH and CCl_3COOH. Furthermore, when the stannic halides were mixed with β-alanine in the ratio 1 : 2 in CH_3COOH, the compounds $SnX_4 \cdot 2AcH \cdot 2\beta\text{-AnH}$ and $[SnX_6](\beta\text{-AnH}_2)_2$ were formed. From a mixture of stannic bromide with β-alanine in CH_3COOH in the ratio 1 : 4 a viscous liquid separated out, analysis of which showed that it was the compound $SnBr_4 \cdot 4\beta\text{-AnH}$. The complex compound $SnCl_4 \cdot 4\beta\text{-AnH}$ was obtained by displacement of two molecules of CH_3COOH by alanine from the compound $SnCl_4 \cdot 2AcH \cdot 2\beta\text{-AnH}$. The compound $SnBr_4 \cdot 2\beta\text{-AnH}$ was obtained by mixing the components in the ratio 1 : 2 in the absence of a solvent. When we attempted to prepare the compound $SnCl_4 \cdot 2\beta\text{-AnH}$ by displacement of CCl_3COOH by stannic chloride from alanine trichloroacetate, apparently the addition product $SnCl_4 \cdot 2CCl_3COOH \cdot 2\beta\text{-AnH}$ was obtained.

We also carried out the cryoscopic titration of β-alanine with stannic chloride and bromide in CH_3COOH and CCl_3COOH (Figs. 1 and 2). When stannic chloride (or bromide)** was added to a solution of β-alanine in CH_3COOH, we observed a decrease in the depression [ΔT] up to 50 mole % [of the stannic halide], but on further addition of stannic chloride the depression increased sharply. The equivalence point corresponds to 50 mole % and the depression at this point is a little more than 1/2 of the initial value, which confirms the presence of solvolysis in the system and the suggested mechanism of solvolysis. Actually, from consideration of Equation (4) it follows that when the stannic halides act on a solution of the amino acid in CH_3COOH (in view of the fact that CH_3COOH is the solvent and that $[SnX_6](\beta\text{-AnH}_2)_2$ separates out in the precipitate), the number of particles decreases, since as a result of the reaction one molecule of $SnX_2(CH_3COO)_2$ appears in the solution in place of two molecules of the amino acid. The equivalence point should be at the equimolecular composition, since two molecules of the stannic halide are expended for two molecules of amino acid.

* The compound $SnCl_4 \cdot 4\alpha\text{-AnH}$ has been described in the literature [3].

** The solvolysis does not go to completion.

TABLE 2

Ratio SnX_4 : β-AnH	Found (%) Sn	Found (%) Cl (Br)	Composition of compound	Calculated (%) Sn	Calculated (%) Cl(Br)	Solvent	Remarks
Stannic chloride – β-alanine							
1 : 1	23.16 23.36 23.42 23.81	40.69 40.62 40.61	$[SnCl_4](3\text{-}AnH_3)_2$	23.20	41.58	CH_3COOH	Crystals
1 : 2	23.38 23.36 23.37	41.10 40.73 39.87	$[SnCl_4](3\text{-}AnH_3)_2$	23.20	41.58	CCl_3COOH	Crystals
1 : 2	21.78 21.64 21.62 21.58	25.61 25.50 25.22 25.58	$SnCl_4 \cdot 2AcH \cdot 2\beta\text{-}AnH$	21.24	25.38	CH_3COOH	Crystals
1 : 2	23.80 23.92 23.69 23.47 23.84 23.81	41.44 41.55 41.02 41.45 41.52 41.62	$[SnCl_4](3\text{-}AnH_3)_2$	23.20	41.58	CCl_3COOH	Crystals
1 : 2	15.76 15.85 15.93 15.93	18.84 18.88 18.46 18.36	$SnCl_4 \cdot 2CCl_3COOH \cdot 2\beta\text{-}AnH$	15.50	18.52		Action of $SnCl_4$ on alanine trichloroacetate
1 : 4	23.56 23.51 23.63	41.12 41.37 40.04	$[SnCl_4](3\text{-}AnH_3)_2$	23.20	41.58	CCl_3COOH	Crystals
1 : 4	19.00 19.27 19.27 19.28	22.67 22.73 22.83 22.76 22.47 22.40	$SnCl_4 \cdot 4\beta\text{-}AnH$	19.24	23.06		By the action of alanine on the compound $SnCl_4 \cdot 2AcH \cdot 2\beta\text{-}AnH$
Stannic bromide – β-alanine							
1 : 1	15.88 15.51 15.58	61.81 61.15 61.57 61.16	$[SnBr_4](3\text{-}AnH_3)_2$	15.24	61.60	CH_3COOH	Crystals
1 : 1	16.60 16.60	61.12 60.93	$[SnBr_4](3\text{-}AnH_3)_2$	15.24	61.60	CCl_3COOH	Crystals
1 : 2	16.87 16.31 16.62 16.28	43.96 43.22 43.72 43.45	$SnBr_4 \cdot 2AcH \cdot 2\beta\text{-}AnH$	16.11	43.44	CH_3COOH	Viscous liquid crystallizing on standing
1 : 2	18.89 19.03 18.73 18.79 18.68 18.53	51.43 51.37 51.42 51.20 51.09 51.71	$SnBr_4 \cdot 2\beta\text{-}AnH$	19.25	51.84		In absence of solvent
1 : 4	14.46 14.47 14.79	39.21	$SnBr_4 \cdot 4\beta\text{-}AnH$	14.93	40.22	CH_3COOH	Viscous liquid

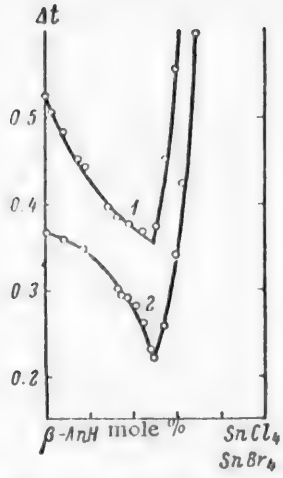

Fig. 1. Cryoscopic titration of β-alanine with stannic bromide (1) and stannic chloride (2) in CH_3COOH.

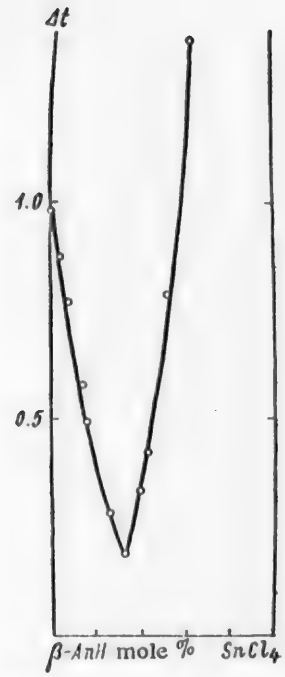

Fig. 2. Cryoscopic titration of β-alanine with stannic chloride in CCl_3COOH.

In the cryoscopic titration of β-alanine with stannic chloride in CCl_3COOH (Fig. 2) the formation of precipitate was observed and a decrease in the depression up to 33 mole % of $SnCl_4$, after which the depression increased. The change in the depression in the system indicates the formation of the compound $SnCl_4 \cdot 2CCl_3COOH \cdot 2\beta\text{-AnH}$.

The Systems $SnCl_4$–LeuH* and $SnBr_4$–LeuH

In Table 3 the results are given for the analysis of the reaction products obtained in the reaction of $SnCl_4$ and $SnBr_4$ with leucine in CH_3COOH and CCl_3COOH.

The results of the analysis show that when $SnCl_4$ and $SnBr_4$ were mixed with leucine in CH_3COOH, the compounds $[SnCl_6](LeuH_2)_2$ and $[SnBr_6](LeuH_2)_2$ were formed. From a mixture of 1 : 2 composition crystals of $(LeuH)_2 \cdot HCl$ and $(LeuH_2)_2 \cdot HBr$ precipitated on prolonged standing. The formation of all these reaction products indicates that when the stannic halides react with leucine in CH_3COOH, solvolysis takes place. Along with this process, the formation of the complexes $SnX_4 \cdot 4LeuH$ and $SnX_4 \cdot 2AcH \cdot 2LeuH$ takes place.

The Systems $SnCl_4$–GlH and $SnBr_4$–GlH

When stannic chloride and bromide acted on solutions of α- and β-alanine, and also leucine in CH_3COOH and in CCl_3COOH, we obtained the complex compounds $[SnX_6](AmH_2)_2$, $SnX_4 \cdot 2AcH \cdot 2AmH$, $SnX_4 \cdot 4AmH$, and SnX_4 2AmH.

Previously, in a study of the reaction of $SnCl_4$ and $SnBr_4$ with glycine we isolated complex compounds analogous in composition to the last three. We did not find the compound $[SnX_6](AmH_2)_2$, and we therefore returned to a study of the reaction of glycine with stannic chloride and bromide in different solvents (CH_3COOH, CCl_3COOH, and CH_3NO_2).

In Table 4 the results of the analysis of the reaction products are given.

From a consideration of the results of the analysis it can be seen that when stannic chloride was mixed with solutions of glycine in nitromethane and in acetic acid (in the ratios 1 : 1 and 1 : 2), the complex compounds $[SnCl_6] \cdot (GlH_2)_2$ and $SnCl_4 \cdot 2AcH \cdot 2GlH$ were formed, and also glycine hydrochloride. Analogous reaction products were

* LeuH is leucine.

TABLE 3

Ratio SnX_4 : LeuH	Found (%) Sn	Found (%) Cl(Br)	Composition of compound	Calculated (%) Sn	Calculated (%) Cl(Br)	Solvent	Remarks
Stannic chloride– leucine							
1 : 1	17.92 18.06 17.75 17.66 16.83	28.89 28.61 28.39 29.08	$[SnCl_4](LeuH_3)_2$	19.92	35.71	CH_3COOH	Crystals Ratio Sn: Cl = 5.42
1 : 2	— — —	11.84 11.72 11.92	$(LeuH)_2 \cdot HCl$	—	11.86	CH_3COOH	Crystals
1 : 2	18.29 18.33 18.75 18.34 18.62	21.81 21.75 21.63 21.82	$SnCl_4 \cdot 2AcH \cdot 2LeuH$	18.46	22.08	CH_3COOH	Viscous liquid
1 : 2	16.05 15.74	18.91 18.79	$SnCl_4 \cdot 2CCl_3COOH \cdot 2LeuH$	14.48	17.30	—	Action of $SnCl_4$ on leucine trichloroacetate
1 : 4	15.31 15.65 15.26 15.80	18.10 17.91 18.16 17.86	$SnCl_4 \cdot 4LeuH$	15.11	18.06	—	Action of leucine on the compound $SnCl_4 \cdot 2AcH \cdot 2LeuH$
Stannic bromide– leucine							
1 : 1	13.52 13.62 13.48	55.65 55.85 55.72	$[SnBr_4](LeuH_3)_2$	13.76	55.59	CH_3COOH	Crystals
1 : 2	14.04 14.41	38.29 38.89 38.87 38.95	$SnBr_4 \cdot 2AcH \cdot 2LeuH$	14.46	38.95	CH_3COOH	Crystals
1 : 2	— — —	23.46 23.12 23.24	$(LeuH)_2 \cdot HBr$	—	23.28	CH_3COOH	Crystals
1 : 2	16.36 16.66 16.76	45.19 44.51 45.13 44.92 45.29	$SnBr_4 \cdot 2LeuH$	16.94	45.62	—	In absence of solvent
1 : 4	12.83 12.51 12.74 12.50 12.59	31.81 32.27 32.73 32.69 32.45	$SnBr_4 \cdot 4LeuH$	12.32	32.18	CH_3COOH	Viscous liquid

TABLE 4

Ratio SnX_4 : GlH	Found (%) Sn	Found (%) Cl(Br)	Composition of compound	Calculated (%) Sn	Calculated (%) Cl(Br)	Solvent	Remarks
Stannic chloride – glycine							
1 : 1	24.20	42.46	$[SnCl_4](GlH_2)_2$	24.54	43.99	CH_3NO_2	Crystals
	24.36	—					
	24.18	—					
1 : 1	—	27.12	$SnCl_4 \cdot 2AcH \cdot 2GlH$	22.36	26.76	CH_3COOH	
	—	26.76					
1 : 2	—	39.93	$[SnCl_4](GlH_2)_2$	24.54	43.99	CH_3COOH	
1 : 2	1.10	—	$(GlH)_2 \cdot HCl$		19.00		
Stannic bromide – glycine							
1 : 1	15.95	62.42	$[SnBr_4](GlH_2)_2$	15.82	61.90	CCl_3COOH	Crystals
	15.90	61.00					
1 : 2	15.90	62.42	$[SnBr_4](GlH_2)_2$	15.82	61.90	CH_3COOH	Crystals
1 : 2	16.19	44.71	$SnBr_4 \cdot 2AcH \cdot 2GlH$	16.75	45.11	CH_3COOH	
	16.42	44.80					
	16.27	44.76					
1 : 2	—	34.88	$(GlH)_2 \cdot HBr$	—	34.59	CH_3COOH	Crystals
	—	34.42					
	—	34.43					
	—	34.46					
1 : 2	19.13	54.10	$SnBr_4 \cdot 2GlH$	20.16	54.31		In absence of solvent
	17.45	54.05					
1 : 4	14.85	38.09	$SnBr_4 \cdot 4GlH$	16.07	43.23		
	14.24	—					

obtained when stannic bromide acted on glycine in CH_3COOH and CCl_3COOH. Furthermore, the compound $SnBr_4 \cdot 2GlH$ was obtained, which we were unable to isolate in good time. This compound was obtained by the action of stannic bromide on the crystalline compound $GlH \cdot CCl_3COOH$. Upon heating, we observed the displacement of CCl_3COOH and the formation of a clear viscous liquid. After washing of this viscous liquid with hot benzene and subsequent removal of the benzene, we obtained a glassy mass. Analysis of this mass showed that its tin and bromine content corresponded to the compound $SnBr_4 \cdot 2GlH$. When the compound was dissolved in CH_3COOH, a clear viscous liquid was formed, from which needle-shaped crystals separated on prolonged standing. Analysis of these crystals corresponded to the composition of the compound $SnBr_4 \cdot 2AcH \cdot 2GlH$, which we had obtained previously [1]. When the compound $SnBr_4 \cdot 2GlH$ was dissolved in excess CH_3COOH and the solution was heated, a crystalline product was formed, in which we found no traces of tin and the bromine content of which corresponded to the compound $(GlH)_2 \cdot HBr$.

Thus, these data show that with glycine, in addition to the complex-forming reactions, solvolysis takes place, as with alanine and leucine.

SUMMARY

1. The reaction of the halides of tetravalent tin with glycine, leucine, and α- and β-alanine in different solvents (CH_3COOH, CCl_3COOH, and CH_3NO_2) has been studied. It has been established that along with the compounds $SnX_4 \cdot 2AmH$, $SnX_4 \cdot 4AmH$, and $SnX_4 \cdot 2BH \cdot 2AmH$, the compounds $[SnX_6](AmH_2)_2$ and $SnX_2(B)_2$ are formed, where X = Cl or Br, AmH is an amino acid molecule, and BH is a solvent molecule.

2. It has been shown that when the stannic halides act on the amino acids in such solvents as CH_3COOH, CCl_3COOH, and CH_3NO_2, solvolysis takes place, along with the complex-forming reactions. The presence of solvolysis has been confirmed by the reaction products isolated and by cryoscopic investigation.

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ORIENTATION IN SUBSTITUTION IN THE AROMATIC NUCLEUS

VI. ORIENTATION OF THE SULFO GROUP IN THE SULFONATION OF TOLUENE

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Many reactions of substitution in the aromatic nucleus may go both as reversible and as practically irreversible reactions by changing the conditions under which they are run. Thus, the reactions of sulfonation, alkylation, halogenation, and in some cases even of nitration [1] may proceed both reversibly and irreversibly depending on the conditions. If the substitution reactions proceed under conditions where they are reversible, then the result of the substitution reactions frequently stands outside the frame of the classical rules of orientation in the benzene nucleus. The character of substitution reactions depends mainly on the temperature. Thus, aromatic sulfonic acids are not hydrolyzed at low temperatures, and the sulfonation reaction proceeds in a practically irreverisble manner. When the temperature is raised, sulfonic acids acquire the ability of being hydrolyzed at a measurable speed, and the sulfonation reaction proceeds in a reversible manner.

The results of studying the sulfonation of toluene under various conditions are discussed in the present paper.

In the 90 years elapsing since the isolation of o- and p-toluenesulfonic acids by Engelhardt and Lachinov [2], a large number of papers has been devoted to a study of the sulfonation of toluene. However, even at the present time a study of the process of formation of the isomers remains far from being complete. After it was discovered by Claesson [3] that m-toluenesulfonic acid is present in the sulfonation product of toluene, the question as to its amount led to controversy in the old papers until the paper by Holleman and Caland appeared [4]. It was shown by these authors that when the temperature is raised from 0 to 100° the amount of the o-isomer decreases in round numbers from 50 to 15%, that of the p-isomer increases from 57 to 78%, while the amount of the m-isomer increases from 3 to 10%. Both the ratio of the reactants and the concentration of the sulfuric acid used also exert an influence on the ratio of the isomers, but to a much less degree than the temperature. The question of the amount of m-isomer formed was not touched upon in later papers on the sulfonation of toluene. Attempts to sulfonate toluene at temperatures considerably above 100° showed essentially nothing [5].

First of all we examined the hydrolysis of the isomeric toluenesulfonic acids under various conditions. The results of the experiments, given in Table 1, indicate that only the o-isomer is noticeably hydrolyzed at 100°. All three isomers are hydrolyzed at 137°. The hydrolysis goes at a much faster rate at 155°. Consequently, the reaction for the sulfonation of toluene becomes reversible at a temperature somewhat below 137°.

The results of the experiments on the sulfonation of toluene are given in Table 2. At 0° the reaction of chlorosulfonic acid with toluene (7 ml per 3 g), as the result of the primary act of the sulfo group entering the ring, yields approximately equal amounts of the o- and p-isomers and about 4% of the m-isomer. At 100° the p-isomer predominates due to hydrolysis of the o-isomer and resulfonation of the toluene. The amount of m-isomer increases very slowly and only after 400 hr does it reach 8%. At 128° the reaction is reversible. Here the more stable m-isomer tends to accumulate, and in less than 850 hr the system reaches a state that is close to the equilibrium between the isomers. Further reaction does not change the composition of the equilibrium mixture.

TABLE 1

Hydrolysis of Toluenesulfonic Acids in Hydrochloric Acid for 25 Hours

Toluenesulfonic acid	HCl concentration (in %)	Moles H_2O / mole sulfonic acid	Temperature	Amount hydrolyzed, %
Ortho-	31.2	4.47	100°	0.6
Para-	27.5	5.36	100	0
Meta-	30.4	4.65	100	0
Ortho-	31.3	4.51	137	10.6
Para-	30.8	4.55	137	4.7
Meta-	31.2	4.48	137	0.2
Ortho-	32.2	4.27	155	93.9
Para-	31.1	4.50	155	49.4
Meta-	32.3	4.24	155	3.2

TABLE 2

Sulfonation of Toluene with 94.2% Sulfuric Acid

Expt. No.	Temperature	Time, hr	F. p. of obtained chloride	Composition of mixed toluenesulfonic acids, %		
				ortho-	para-	meta-
1	101°	4	56.8°	16.6	80.0	3.4
2		25	60.0	10.4	86.0	3.6
3		100	60.5	7.4	87.0	5.6
4		400	57.9	9.8	82.0	8.2
5	128	88	45.6	6.6	60.1	33.3
6		288	37.8	3.3	49.8	46.9
7		847	31.0	2.5	41.8	55.7
8		1687	30.2	3.5	41.0	55.5
9	162	4	50.5	7.8	68.2	24.0
10		12	45.8	4.0	60.4	35.6
11		25	36.2	4.2	47.8	48.0
12		50	31.8	3.3	42.7	54.0
13		70	29.2	7.1	39.8	53.1
14	181	4	40.7	8.6	53.2	38.2
15		8	38.7	8.1	50.8	41.1
16		11	29.9	7.2	40.5	52.3
17		16	29.4	5.8	40.5	54.2
18		27	32.2	4.3	43.2	52.5
19	200	1	39.6	7.9	52.0	40.1
20		2	—	—	—	49.4
21		3	32.0	2.9	43.0	54.1
22		4	30.0	4.5	40.7	54.8

In the three following series of experiments the sulfonation was run at 162, 181 and 200°. For all practical purposes the equilibrium state in these three series of experiments was reached in about 40-50, 11-12 and 3 hours, respectively, with the equilibrium mixture containing, on the average, 54% m-, 41% p- and 5% of the o-isomer. It is possible that the composition of the equilibrium mixtures changes when the temperature is varied from 128 to 200°, but this change lies within the limits of accuracy of the method used for the quantitative determination of the isomeric toluenesulfonic acids.

TABLE 3

Isomerization of Toluenesulfonic Acids in 81% Sulfuric Acid at 160°

Toluenesulfonic acid	Duration of heating, hr	Composition of mixed toluenesulfonic acids, %		
		ortho-	para-	meta-
Para-	40	12.3	46.8	40.9
	100	9.2	35.5	55.3
Meta-	50	4.9	34.0	61.1
	100	7.6	34.4	58.0

TABLE 4

Composition of Equilibrium Mixtures (in %)

Process	Ortho-isomer	Para-isomer	Meta-isomer
Sulfonation of toluene at 128-200°	6	40	54
Sulfonation of chlorobenzene at 185-238°	0	46	54
Isomerization of dichlorobenzenes at 120-180°	16	30	54

We also subjected pure m- and p-toluenesulfonic acids to isomerization by heating them in 81% sulfuric acid. The results of these experiments are given in Table 3. These experiments show that starting with the p-isomer it is possible to reach a state close to equilibrium in 100 hr. The m-isomer, being less reactive, must be heated for a somewhat longer time in order to obtain a mixture of the same composition. As a result, it is also possible to obtain the equilibrium mixture of the isomers by starting with the pure sulfonic acids.

All of the above discussed experiments show that the m-isomer is the most stable, both kinetically and thermodynamically. The o-isomer is the most labile.

Finally, the compositions of the equilibrium mixtures formed in the sulfonation of toluene and of chlorobenzene [6] and also when the dichlorobenzenes are isomerized in the presence of aluminum chloride [7] are given in Table 4. In all cases the equilibrium system is observed to contain about 54%, i.e., a constant and predominant amount of the m-isomer. This indicates that chlorine and the methyl group are similar in their orienting influence in the benzene nucleus. The variation in the amounts of the o-isomer formed in the three processes cited above is explained by steric factors.

Actually, the halogenating chloro-ion is smaller in size than either the sulfonating HSO_3^+ or $H_3SO_4^+$ ion, which makes it possible to form 16% of o-dichlorobenzene in the equilibrium mixture. The sulfonation of toluene gives about 5% of the o-isomer, since the methyl group occupies a small space; the sulfonation of chlorobenzene leads to the practically complete absence of the o-isomer, since the chlorine in the nucleus occupies a greater volume than the methyl group.

As a result, the results obtained in the sulfonation of toluene and chlorobenzene, and also in the isomerization of the dichlorobenzenes at elevated temperatures (100-238°), do not fit into the frame of the classical rules regarding orientation in the benzene nucleus. The orientation rules retain their significance under those conditions where the substitution reactions proceed in a practically irreversible manner, or if the reaction is a long way from the equilibrium state. In substitution reactions, proceeding under conditions of reversibility, in the presence of

orienting substituents of the 1st type in the nucleus, predominant m-orientation is observed in a number of cases due to the accumulation of the more stable m-isomer in the reaction mixture, the amount of which in a state close to equilibrium may be very high or even predominant.

EXPERIMENTAL

The pure o-, m- and p-toluenesulfonic acids were obtained from the corresponding toluenesulfonyl chlorides, the preparation of which was described earlier [8]. The chlorides were hydrolyzed in 70% alcohol under reflux, and then the solutions were evaporated until the test for chloride ion was negative. The amount of water in the sulfonic acids was determined alkalimetrically.

To study the hydrolysis of the sulfonic acids, the mixture of weighed chloride and water, taken in the proportions of 5.5 moles of water per mole of chloride, was placed in a test tube, which was sealed, and then the chloride was hydrolyzed by heating on the water bath with frequent shaking for 2-3 hours. The time when the mixture became homogeneous was taken as the start of the experiment. The amount of hydrolyzed sulfonic acid was established by the amount of sulfuric acid formed, which was determined gravimetrically.

The toluene used in the sulfonation experiments was obtained from pure p-toluenesulfonyl chloride, which was hydrolyzed to the sulfonic acid, as described above, and then the latter was hydrolyzed in 70% phosphoric acid by passing steam through the mixture at 160-180°. The toluene that steam-distilled was dried and distilled.

For the sulfonation experiments a mixture of 1.5 g of toluene and 4.25 g of 94% sulfuric acid was sealed in a test tube, the test tube heated on the water bath with shaking until the mixture ceased to stratify, and then the mixture was heated in an Eyckmann apparatus. We used 3.5 g of sulfuric acid in the experiments that were run at 181 and 200°. The temperature varied within ±1° of that indicated in Table 2. The sulfonation mixture was analyzed by the earlier-described method [8].

In some of the experiments the sulfonation mixture was poured into water in order to determine the amount of sulfones and insoluble tars, which were determined by filtration, drying, and weighing. Then using barium carbonate and sodium sulfate, the sulfuric acid was removed from the solution, while the toluenesulfonic acids were converted to the sodium salts, and the latter by reaction with phosphorus pentachloride were converted to the mixed sulfonyl chlorides. Thus, in Expt. 16 (Table 2) the amount of sulfones and tars represented 1.3% of the weight of the sulfonation mixture. The mixed sulfonyl chlorides were obtained in 79% yield (based on toluene taken). In Expt. 19 the amount of sulfones and tars was 1.54%, and in Expt. 20 it was 1.6% of the weight of mixed toluenesulfonic acids.

P. T. Pestova assisted in the work.

SUMMARY

Experiments on the hydrolysis of o-, m- and p-toluenesulfonic acids in 30% hydrochloric acid revealed that only the o-isomer is hydrolyzed at 100°. Hydrolysis of all of the isomers is observed at around 130°. The reactivity in the hydrolysis decreases in the order o- > p- > m-.

The sulfonation of toluene at 128° and higher leads to an equilibrium mixture of the isomers, containing 5% o-, 41% p- and 54% m-isomer. A state close to the equilibrium is reached in 3 hr at 200°, in 11 hr at 181°, etc.

A mixture of isomers having a composition close to that of the equilibrium mixture was also obtained by heating the pure p- and m-toluenesulfonic acids in 81% sulfuric acid.

As a result, predominantly m-orientation is observed under conditions where the sulfonation of toluene is reversible. This is due to the accumulation of the more stable m-isomer in the reaction mixture, which does not fit into the frame of the classical rules regarding orientation in the benzene nucleus.

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REACTIONS OF MAGNESYLAMINES

VIII. SYNTHESIS AND PROPERTIES OF ARYLAMIDES OF N-ARYL(ALKYL)- AND N-ACYL-SUBSTITUTED ANTHRANILIC ACIDS

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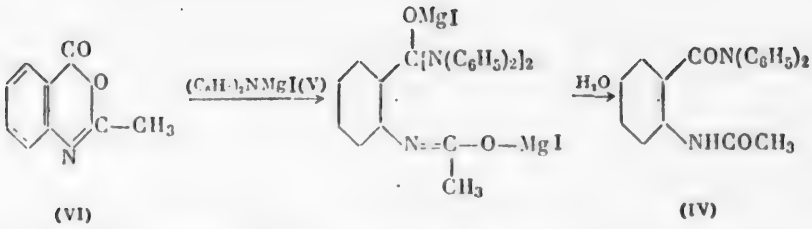
In recent years great interest is shown in the N-substituted amides of various carboxylic acids as being compounds with possible biological activity. In this respect a definite interest is possessed by the N-arylamides of aromatic amino acids, and, in particular, by the derivatives of anthranilic acid. According to [1], the diethylaminoethylamide of triphenylamine-2-carboxylic acid exhibits spasmolytic activity, while the synthesis of the corresponding acridine derivative [2] was accomplished by starting with the diethylaminoethylamide of diphenylamine-2-carboxylic acid.

According to the literature [1], the arylamides of N-aryl-substituted anthranilic acids may be obtained by reacting the halides of the corresponding acids with amines, and belong in the class of little-studied compounds. The arylamides of N-acylanthranilic acids possess interest as starting materials for the synthesis of quinazolone compounds [3].

In an earlier paper [4] we investigated the possibility of extending the reaction between magnesylamines and esters to the ester of N-aryl(alkyl)- and N-acyl-substituted anthranilic acids for the purpose of obtaining the amides of these acids and making a study of their properties. The starting esters (I) taken for these syntheses were obtained either by the esterification of N-aryl(alkyl)-anthranilic acids or by the acylation of methyl anthranilate. Since the esters of N-aryl(alkyl)- and N-acyl-anthranilic acids contain a labile hydrogen atom (the hydrogen of the NH group), it was necessary to establish the most favorable conditions for running the synthesis. Experiments revealed that the highest yields of reaction products are obtained in the case where 1.5 moles of dimagnesylamine is taken per mole of ester. The experimental results are given in Tables 1 and 2, and from this data it can be seen that the arylamides of N-aryl(alkyl)- and N-acyl-anthranilic acids (II) are obtained in yields up to 90% and higher, which permits recommending the reaction studied by us as being a good way of synthesizing the indicated compounds. The method is suitable for the synthesis of both primary and secondary arylamides. It should be mentioned that the reaction goes with greater difficulty with (I) than with methyl anthranilate. Thus, in the case of methyl anthranilate the reaction is ended in 30 min, whereas to complete the reaction with (I) requires at least 1 hour.

Steric hindrance increases greatly in going from (I) to N-disubstituted methyl anthranilate. Thus, in general, the methyl ester of triphenylamine-2-carboxylic acid does not react with dimagnesylamines. The experiments were run with N,N-bis(bromomagnesium)aniline in ether, benzene, pyridine, and dioxane media.

Further, it was shown that the reaction between magnesylamines and N-acylanthranil may be used successfully to synthesize arylamides of N-acylanthranilic acids. For example, the diphenylamide of N-acetylanthranilic acid (IV) is formed in nearly quantitative yield when diphenylaminemagnesium iodide (V) is reacted with N-acetylanthranil (VI).



(VI) (IV)

Some of the compounds obtained by us were tested pharmacologically. Local anesthetic action was shown by (VII), (VIII) and (IX), but not as potent as that shown by anesthesine.•

EXPERIMENTAL••

Methyl ester of diphenylamine-2-carboxylic acid (XI). A mixture of 37 g of diphenylamine-2-carboxylic acid, 220 ml of methanol and 20 ml of concd. sulfuric acid was heated under reflux for 5 hr on the water bath. The excess alcohol was distilled off, and the residue was poured into water, neutralized with sodium carbonate, and extracted with ether. The ether extract was dried over calcium chloride, after which the ether was distilled on the water bath, and the residue was vacuum-distilled, b.p. 180-181° at 10 mm. The obtained product was recrystallized from ligroine. Prisms with m.p. 59°. Yield 37.7 g (95.8%). Literature data: m.p. 111° [7]. Our experiments on the preparation and various ways of purifying (XI) do not support the data of [7].

Methyl ester of N-butylanthranilic acid (III). Starting compounds: 20 g of N-butylanthranilic acid, 60 ml of methanol and 25 ml of concd. sulfuric acid. The mixture was heated for 12 hr and then worked up as described in the preceding experiment; yield 18 g (84%).

B.p. 164-165° (17 mm), d_{20}^{20} 1.0503.

Found %: N 6.60, 6.77. $C_{12}H_{17}O_2N$. Calculated %: N 6.76.

Anilide of diphenylamine-2-carboxylic acid (X). To the N,N-bis(iodomagnesium)aniline, obtained in conventional manner from 23.4 g of ethyl iodide, 3.6 g of magnesium and 7 g of aniline in 70 ml of ether, was added an ether solution of 11.35 g of (XI). The mixture was heated for 1 hr and then decomposed with dilute hydrochloric acid. The ether layer was separated and the ether was steam-distilled. Yield 13 g. The constants of the obtained compounds are given in Table 1.

Anilide of N-acetylanthranilic acid (XII). The reaction was run in the same manner as described in the preceding experiment. Starting compounds: 6.5 g of ethyl bromide, 1.44 g of magnesium, 2.8 g of aniline and 3.86 g of methyl N-acetylanthranilate (XIII). Yield 3.3 g.

Diphenylamide of N-acetylanthranilic acid (IV). To the (V), obtained from 6.24 g of ethyl iodide, 0.96 g of magnesium and 6.76 g of diphenylamine in 30 ml of ether, was added an ether solution of 3.18 g of (VI), after which the mixture was heated for 20 min and then decomposed with dilute hydrochloric acid. The obtained precipitate was filtered and recrystallized from alcohol. Prisms with m.p. 175-176°. Yield 6.5 g (about 100%).

Found %: C 76.31, 76.27; H 5.72, 5.52; N 8.59, 8.69. $C_{21}H_{18}O_2N_2$. Calculated %: C 76.36; H 5.45; N 8.48.

SUMMARY

1. A study was made of the reaction between the methyl esters of N-aryl(alkyl)- and N-acyl-anthranilic acids and magnesylamines, the latter obtained from both primary and secondary aromatic and alkaromatic amines.

2. It is possible to recommend the indicated reaction as a way of synthesizing the arylamides of N-aryl(alkyl)- and N-acyl-anthranilic acids.

3. It was shown that the reaction between magnesylamines and N-acylanthranil may be used to synthesize the arylamides of N-acylanthranilic acids in good yields.

4. It was established that the steric hindrance in going from the N-mono- to the N-disubstituted esters of anthranilic acid increases so greatly that it becomes practically impossible to aramidate such esters.

• The tests were performed by E. M. Koz'minykh.

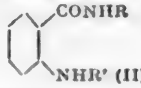
•• With the assistance of student V. V. Dikopolovaya.

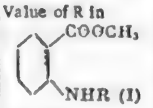
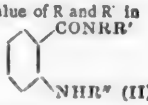
TABLE 1

Melting point	Found (%)			Empirical formula	Calculated (%)			Yield (%)
	C	H	N		C	H	N	
118—119°; Plates	78.93, 79.09	5.65, 5.66	9.93, 9.81	$C_{15}H_{13}ON_3$	79.15	5.55	9.72	90.3
119—120; Needles	79.20, 79.36	6.09, 5.93	9.20, 9.45	$C_{20}H_{15}ON_3$	79.47	5.96	9.27	96
125 [1]: Needles	—	—	—	$C_{15}H_{13}ON_3$	—	—	—	80
84—86: Plates	74.79, 74.99	6.70, 6.74	11.71, 11.80	$C_{15}H_{15}ON_3$	75.00	6.66	11.66	59
125—127; Needles	75.17, 75.13	6.90, 5.88	11.62, 11.70	$C_{15}H_{15}ON_3$	75.00	6.66	11.66	72.2
122—123: Needles	75.58, 75.69	7.03, 7.11	11.01, 10.92	$C_{16}H_{17}ON_3$	75.59	7.08	11.02	81
98—99; Needles	76.25, 75.90	7.76, 7.47	10.62, 10.61	$C_{17}H_{19}ON_3$	76.11	7.46	10.44	45
96—97: Needles	77.15, 76.83	8.20, 8.10	9.50, 9.35	$C_{19}H_{21}ON_3$	77.03	8.11	9.46	57
165; Plates	—	—	11.06, 10.97	$C_{15}H_{14}O_2N_2$	—	—	11.02	82.5
162; Needles	—	—	10.88, 11.17	$C_{15}H_{14}O_2N_2$	—	—	11.02	48
155—156; Needles	—	—	10.50, 10.40	$C_{15}H_{14}O_2N_2$	—	—	10.37	57
167—168 [2]: Needles	—	—	—	$C_{15}H_{14}O_2N_2$	—	—	—	64.7
167—168: Plates from acetone and CCl_4	—	—	10.45, 10.62	$C_{15}H_{16}O_2N_2$	—	—	10.44	82
185—186; Rhombic crystals	—	—	20.25, 10.65	$C_{15}H_{15}O_2N_3$	—	—	10.44	71
278 [3]: plates from toluene	—	—	—	$C_{20}H_{16}O_2N_2$	—	—	—	85.4
219—220; plates from toluene	—	—	8.50, 8.35	$C_{21}H_{18}O_2N_2$	—	—	8.48	91
205—206: plates from toluene	—	—	8.52, 8.62	$C_{21}H_{18}O_2N_2$	—	—	8.48	77

TABLE 2

Melting point	Found (%)			Empirical formula	Calculated (%)			Yield (%)
	C	H	N		C	H	N	
68—69°; plates from ligroin	74.87, 75.05	6.70, 6.84	11.69, 11.84	$C_{15}H_{15}ON_3$	75.00	6.66	11.66	90.3
129—130; plates from alcohol	79.37, 79.26	6.03, 6.01	9.24, 9.28	$C_{20}H_{17}ON_3$	79.47	5.96	9.27	83.3

Value of R		Value of R and R' in 	Name of compound
$RN(MgX)_2$	(I)		
C_6H_5	C_6H_5 (XI)	R and R'=C_6H_5 (X)	Anilide of diphenylamine-2-carboxylic acid
o-$CH_3C_6H_4$	C_6H_5	R=o-$CH_3C_6H_4$; R'=C_6H_5	o-Toluidide of diphenylamine-2-carboxylic acid
C_6H_5	CH_3	R=C_6H_5; R'=CH_3	Anilide of N-methyl-2-aminobenzoic acid
$C_6H_5CH_2$	CH_3	R=$C_6H_5CH_2$; R'=CH_3	Benzylamide of N-methyl-2-aminobenzoic acid
p-$CH_3C_6H_4$	CH_3	R=p-$CH_3C_6H_4$; R'=CH_3	p-Toluidide of N-methyl-2-aminobenzoic acid
C_6H_5—CH(CH$_3$)—	CH_3	R=C_6H_5—CH(CH$_3$)—; R'=CH_3 (VII)	α-Phenylethylamide of N-methyl-2-aminobenzoic acid
C_6H_5—CH(CH$_3$)—	C_2H_5	R=C_6H_5—CH(CH$_3$)—; R'=C_2H_5 (VIII)	α-Phenylethylamide of N-ethyl-2-aminobenzoic acid
C_6H_5—CH(CH$_3$)—	n-C_4H_9 (III)	R=C_6H_5—CH(CH$_3$)—; R'= n-C_4H_9 (IX)	α-Phenylethylamide of N-n-butyl-2-aminobenzoic acid
o-$CH_3C_6H_4$	HCO	R=o-$CH_3C_6H_4$; R'=HCO	o-Toluidide of N-formyl-2-aminobenzoic acid
p-$CH_3C_6H_4$	HCO	R=p-$CH_3C_6H_4$; R'=HCO	p-Toluidide of N-formyl-2-aminobenzoic acid
p-$CH_3OC_6H_4$	HCO	R=p-$CH_3OC_6H_4$; R'=HCO	p-Anisidide of N-formyl-2-aminobenzoic acid
C_6H_5	CH_3CO (XIII)	R=C_6H_5; R'=CH_3CO (XII)	Anilide of N-acetyl-2-aminobenzoic acid
o-$CH_3C_6H_4$	CH_3CO	R=o-$CH_3C_6H_4$; R'=CH_3CO	o-Toluidide of N-acetyl-2-aminobenzoic acid
p-$CH_3C_6H_4$	CH_3CO	R=p-$CH_3C_6H_4$; R'=CH_3CO	p-Toluidide of N-acetyl-2-aminobenzoic acid
C_6H_5	C_6H_5CO	R=C_6H_5; R'=C_6H_5CO	Anilide of N-benzoyl-2-aminobenzoic acid
p-$CH_3C_6H_4$	C_6H_5CO	R=p-$CH_3C_6H_4$; R'=C_6H_5CO	p-Toluidide of N-benzoyl-2-aminobenzoic acid
o-$CH_3C_6H_4$	C_6H_5CO	R=o-$CH_3C_6H_4$; R'=C_6H_5CO	o-Toluidide of N-benzoyl-2-aminobenzoic acid

Value of R and R' in $RR'NMgX$	Value of R in  (I)	Value of R and R' in  (II)	Name of compound
R=CH_3; R'=C_6H_5	CH_3	R=CH_3; R'=C_6H_5; R''=CH_3	Methylphenylamide of N-methyl-2-amonobenzoic acid
R=CH_3; R'=C_6H_5	C_6H_5	R=CH_3; R'=C_6H_5; R''=C_6H_5	Methylphenylamide of diphenylamine-2-carboxylic acid

5. A number of previously unknown arylamides of N-aryl(alkyl)- and N-acylsubstituted anthranilic acids, and also the methyl ester of N-butylanthranilic acid, were synthesized and a study made of their properties.

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CYCLIC ACETALS OF HYDROXYCARBONYL COMPOUNDS

XI. REACTION OF METHYLLACTOLIDES OF α-OXO ALCOHOLS OF ALKAROMATIC SERIES WITH AROMATIC ALDEHYDES AND KETONES [1]

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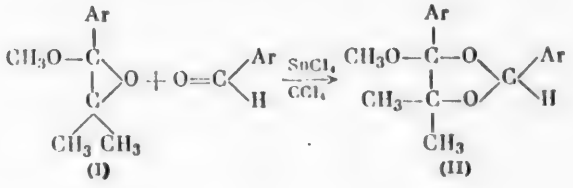
Methyllactolides of α-oxo alcohols, being α-methoxy oxides (I), are capable of undergoing various reactions where the α-oxide ring is opened. In all of the reactions studied up to now the oxide ring opens on the side of the methoxyl group, and derivatives of α-oxo alcohols are formed; in some cases, operating through the methyllactolides, such derivatives have been synthesized as cannot be obtained either from the α-oxo alcohols directly or from the corresponding α-bromoketones; for example, certain mixed ketals [2] and esters [3]. However, this fails to exhaust by far the possibilities of utilizing methyllactolides for synthetic purposes. It is known that α-oxides can be condensed with aldehydes and ketones in the presence of $SnCl_4$ to yield 1,3-dioxolanes [4]. Compounds containing 1,3-dioxolane rings—five-membered cyclic full ketals—are widely used in organic chemistry [1]. 1,3-Dioxolane rings have found their greatest importance in the chemistry of sugars, where investigations were carried out with the acetone and benzylidene derivatives; however, the latter have been studied inadequately. Some fairly well studied compounds, containing 1,3-dioxolane rings and having a methoxyl group in the 2 position, are also known; these compounds are the orthoesters of carbohydrates [5].

As shown by us in the present paper, compounds containing the 1,3-dioxolane ring with a methoxy group in the 4 position (II) may be obtained by reacting methyllactolides with aromatic aldehydes in the presence of $SnCl_4$.



(I) (II)

These compounds are the previously unknown methyl ethers of the benzylidene derivatives of α-oxo alcohol hydrates; to some degree they are analogous to the benzylidene derivatives of monosaccharides. However, it was shown by us that this condensation can be carried out successfully only with the methyllactolides of tertiary α-oxo alcohols. It was also established that the latter can be condensed with aldehydes independently of whether the substituent in the benzene nucleus decreases the positive charge arising on the carbon atom in the opening of the oxide ring (for example, methoxyl) or increases it (for example, chlorine). The electron-chemical character of the substituent found in the p-position of the benzene nucleus of the aromatic aldehyde is also unimportant (H, NO_2, CH_3O). The methyllactolides of tertiary alkaromatic α-oxo alcohols also condense with benzophenone to yield the corresponding 1,3-dioxolanes.

In all cases a colorless, CCl_4-insoluble complex is formed when the aldehyde is added to $SnCl_4$; the color of the solution deepens when the methyllactolide is added, and a new complex soluble in CCl_4 is formed; decomposition of the latter with alkali yields the dioxolane. The same picture is observed when working with the methyllactolides of primary and secondary α-oxo alcohols; however, here after treating the reaction mixture with alkali and water we were able to show the formation of only the corresponding oxo alcohol, the dimerization product of the methoxy oxide (containing the 1,4-dioxane ring), and a small amount of the methoxyketone—the isomerization product of the starting methyllactolide.

Somewhat earlier [6] we had studied the transformations of the methyllactolide of n-propylbenzoylcarbinol in acetone solution containing 2% of water, in the presence of $SnCl_4$, and had shown that partial hydrolysis and partial dimerization of the methoxy oxide to the corresponding substituted dimethoxydioxane take place under these conditions. A condensation product was not found.

In the present paper we were also unable to condense the methyllactolides of secondary α-oxo alcohols (ethylbenzoylcarbinol and n-propylbenzoylcarbinol) and of primary α-oxo alcohols (propionylcarbinol) with either benzaldehyde or benzophenone.

The condensation was carried out by the procedure recommended for the condensation of α-oxides with carbonyl-containing compounds [4]. The structure of the obtained dioxolanes was proved by the elemental analysis results, the character of the absorption in the ultraviolet region of the spectrum, and also by their hydrolysis in acid medium to the starting carbonyl-containing compound and the α-oxo alcohol corresponding to the methyllactolide; treatment with a hot aqueous-alcohol sulfuric acid solution of 2,4-dinitrophenylhydrazine results in instantaneous hydrolysis of the dioxolane and the 2,4-dinitrophenylhydrazone of the aldehyde or ketone deposits, while treating the filtrate with a fresh portion of the hydrazine solution yields the 2,4-dinitrophenylhydrazone of the oxo alcohol, which after purification was identified with the authentic product by mixed melting point.

If the reaction should go in the direction of forming any linear products, then the latter should possess the hydroxyl group and should give the methoxyketone on hydrolysis. However, the test for hydroxyl was negative in all cases.

EXPERIMENTAL

The experiments on the condensation of the methyllactolides of α-oxo alcohols (α-methoxy oxides) with aromatic aldehydes and benzophenone were carried out in the following manner. A solution of the carbonyl-containing compound in CCl_4 was added in drops to a 10% solution of anhydrous $SnCl_4$ in CCl_4; benzophenone forms a soluble complex with $SnCl_4$, while in the other cases the colorless complex is obtained immediately as a precipitate, to which a solution of the methoxy oxide in CCl_4 is then added slowly, in drops, with vigorous stirring. The reaction mixture begins to turn yellow immediately, in some cases subsequently changing gradually to either a dark red or purple; at the same time a colored tarry product deposits on the bottom and on the walls of the flask. The solution is decanted from the precipitate, followed by washing 2-3 times with 20% NaOH solution until the Meissner test for sodium stannate is negative; here the solution decolorizes due to decomposition of the complex, the final product of the reaction with $SnCl_4$. Then the CCl_4 solution is washed with water, dried over fused $MgSO_4$, and the solvent is removed by suction. The residue is obtained either as an oil that gradually crystallizes, or directly as crystals. The tarry deposit represented a mixture of polymerization products and the complex of the starting carbonyl-containing compound with $SnCl_4$; not once were we able to isolate the dioxolane from this tar. The starting products used in the condensation should be pure and completely dry.

1. Reaction of methyllactolide of ethylbenzoylcarbinol with benzaldehyde. The color of the reaction mixture after adding all of the methoxy oxide solution became carmine red; pronounced tarring is observed. Fine white crystals insoluble in CCl_4 collected in the reaction flask; these were separated and recrystallized from methyl alcohol. The crystals represent the methoxy oxide dimer; m.p. 238-239°. The mobile oil remaining after removal of the solvent was fractionally distilled in vacuo. The following fractions were obtained: 1st) b.p. 54-55° at 5 mm—benzaldehyde; 2nd) b.p. 75-96° at 5 mm—mixture of isomerization product of methoxy oxide (methoxyketone) and oxo alcohol; 3rd) b.p. 97-98° at 5 mm—pure oxo alcohol—ethylbenzoylcarbinol, which was identified as the osazone (m.p. 223-224°, from ethanol). The quickly crystallizing oil that remained in the distillation flask proved to be benzoic acid, which was identified both by melting point and by mixed melting point with authentic product.

The described reaction is typical for the methyllactolides of primary and secondary α-oxo alcohols. Numerous attempts were made to change the reaction conditions, not changing, however, the method worked out for the successful experiments: Changes were made in the amount of catalyst, volume of solvent, temperature (from -10° to +60°), and in the manner of removing the solvent (rapid distillation employing heat or employing suction without heat). However, increasing the amount of catalyst, a long heating time, and a rapid removal of the solvent by distillation all favored only an increase in the yield of tarry products and made it difficult to determine the end results of the reaction.

The residue (oil) after removal of the solvent was allowed to stand in order to crystallize; however, after some time we found it necessary to separate the liquid reaction products by fractional distillation in vacuo, since the oil did not crystallize for a long time (in the case of p-nitrobenzaldehyde, for example, the oil did not crystallize even after 27 months).

As a result, we were unable to obtain methoxydioxolanes by the condensation of the methyllactolides of primary and secondary α-oxo alcohols with aromatic aldehydes and benzophenone.

2. Condensation of methyllactolide of dimethylbenzoylcarbinol with carbonyl-containing compounds. The methyllactolide was obtained by the method described in [3].

a) Condensation with benzaldehyde; 5,5-dimethyl-2,4-diphenyl-4-methoxy-1,3-dioxolane. A solution of 2.1 g of benzaldehyde in 10 ml of CCl_4 was added to a solution of 0.3 g of anhydrous $SnCl_4$ in 5 ml of CCl_4, followed by the addition of 4.5 g of the methyllactolide in 20 ml of CCl_4. The reaction mixture assumed a yellow color. Crystals were obtained after the CCl_4 was vacuum-distilled which, after two recrystallizations from aqueous alcohol, had m.p. 98-99° (α-form). If the CCl_4 is distilled off without using heat, then crystals are obtained which, after recrystallization from aqueous alcohol, melt at 84-86° (β-form). Yield 40-50%. Both types of crystals are handsome colorless needles, absolutely analogous in their properties clear down to the identity of their ultraviolet absorption curves. In order to obtain analytically pure compounds, the crystals must be kept in a vacuum-desiccator over $CaCl_2$ for 5-7 days.

α-Form. Found %: C 75.9, 76.2; H 7.24, 7.15; CH_3O 10.61, 11.01. M 279. β-Form. Found %: C 76.2; H 7.31; CH_3O 10.74. $C_{18}H_{20}O_3$. Calculated %: C 76.03; H 7.09; CH_3O 10.91. M 284.3.

The dioxolane can be steam-distilled from alkaline solution; the isolated crystals melted at 98-99°.

b) Condensation with anisaldehyde; 5,5-dimethyl-4-phenyl-2-p-methoxyphenyl-4-methoxy-1,3-dioxolane. The color of the reaction mixture turned to a carmine red when the methyllactolide solution was added. The oil, remaining after removal of the CCl_4 by suction crystallized immediately. Exactly as was done with all of the subsequently described dioxolanes, the obtained dioxolane was recrystallized several times (2-4 times) from aqueous alcohol. The yield of the different dioxolanes ranged from 40 to 50%. The present dioxolane was obtained as well shaped, handsome, colorless needles with m.p. 74-75°.

Found %: C 72.36, 72.40; H 7.09, 7.11; CH_3O 20.02, 19.88. $C_{19}H_{22}O_4$. Calculated %: C 72.58; H 7.05; CH_3O 19.75.

c) Condensation with p-nitrobenzaldehyde; 5,5-dimethyl-4-phenyl-2-p-nitrophenyl-4-methoxy-1,3-dioxolane. The condensation conditions were the same as before. The reaction mixture and solution were faintly yellow The residue oil crystallized very slowly, and the isolated crystals melted over a wide range. Recrystallization from pure alcohol gave the compound as colorless, fine cubic crystals with m.p. 139-140° (α-form); addition of water to the mother liquor gave a precipitate which, recrystallized as usual from aqueous alcohol, gave needle crystals with m.p. 86-88° (β-form).

α-Form: Found %: C 65.58; H 5.91; N 4.36; CH_3O 9.22. β-Form: Found %: C 65.71; H 6.12; N 4.41; CH_3O 9.28. $C_{18}H_{19}O_5N$. Calculated %: C 65.70; H 5.82; N 4.27; CH_3O 9.43.

d) Condensation with benzophenone; 5,5-dimethyl-2,2,4-triphenyl-4-methoxy-1,3-dioxolane. The condensation conditions were the same as before. The complex of $SnCl_4$ with benzophenone is soluble in CCl_4. The addition of the first drops of the methyllactolide caused the solution to become turbid, and a tarry red substance separated. The CCl_4 solution was faintly yellow. The reaction went with slight heat evolution. Tarring was very slight. The crystals that separated from the oil only after standing for a week had m.p. 89-90°.

Found %: C 79.81, 79.84; H 6.94, 6.63; CH_3O 8.68, 8.72. $C_{24}H_{24}O_3$. Calculated %: C 79.97; H 6.71; CH_3O 8.62.

2. Condensation of methyllactolide of dimethyl-p-chlorobenzoylcarbinol with carbonyl-containing compounds. The preparation of the methyllactolide was described in detail in [7].

a) Condensation with benzaldehyde; 5,5-dimethyl-2-phenyl-4-p-chlorophenyl-4-methoxy-1,3-dioxolane. A solution of 4 g of benzaldehyde in 10 ml of CCl_4 was added to a solution of 0.5 ml of $SnCl_4$ in 5 ml of CCl_4, followed by the addition of a solution of 8 g of the methoxy oxide in 10 ml of CCl_4. The color of the reaction mixture was orange. The oil remaining after removal of the CCl_4 crystallized the following day. Colorless needles (from aqueous alcohol), m.p. 85-87°.

Found %: C 67.55, 67.83; H 6.26, 6.05; Cl 11.25, 11.08; CH_3O 9.89, 10.01. $C_{18}H_{19}O_3Cl$. Calculated %: C 67.85; H 6.01; Cl 11.12; CH_3O 9.72.

b) Condensation with benzophenone; 5,5-dimethyl-2,2-diphenyl-4-p-chlorophenyl-4-methoxy-1,3-dioxolane. The condensation conditions were the same as before, and the reactants were taken in equimolar amounts. The oil remaining after removal of the solvent did not crystallize after standing for a long time, but treatment with cold alcohol led to the deposition of fine white crystals of the dioxolane from the solution, which were then recrystallized in the usual way from aqueous alcohol, m.p. 80-82°.

Found %: C 72.97, 72.80; H 5.91, 5.96; Cl 8.81, 8.76; CH_3O 7.91, 7.74. $C_{24}H_{23}O_3Cl$. Calculated %: C 72.99; H 5.87; Cl 8.97; CH_3O 7.85.

3. Condensation of methyllactolide of dimethyl-p-anisoylcarbinol with carbonyl-containing compounds. a) Condensation with anisaldehyde; 5,5-dimethyl-2,4-anisyl-4-methoxy-1,3-dioxolane.* The preparation of the methyllactolide was described in [7]. For the condensation we took 3 g of anisaldehyde (in 5 ml of CCl_4) and 5.2 g of the methyllactolide (in 25 ml of CCl_4). A dark-red tarry liquid was obtained here. After vacuum-distillation of the CCl_4 the residual oil crystallized after standing for 2 months. After two recrystallizations from alcohol the crystals melted at 138.5-139.5°.

Found %: C 70.29, 70.38; H 7.19, 7.31. $C_{20}H_{24}O_5$. Calculated %: C 69.75; H 7.06.

b) Condensation with m-nitrobenzaldehyde; 5,5-dimethyl-2-m-nitrophenyl-4-methoxyphenyl-4-methoxy-1,3-dioxolane.* For the condensation we took 2.3 g of m-nitrobenzaldehyde and 4.05 g of the methyllactolide. The reaction mixture had a yellow color. After the customary treatment and removal of the CCl_4 in vacuo we obtained an oil, which crystallized only after standing for a month. After recrystallization from alcohol the isolated crystals had m.p. 109.5-110.5°.

Found %: C 63.21, 63.29; H 6.19, 6.08. $C_{19}H_{21}O_6N$. Calculated %: C 63.49; H 5.89.

SUMMARY

1. A method was developed for the condensation of α-methoxy oxides with aromatic aldehydes and benzophenone. As the result of the condensation we synthesized some new substituted 1,3-dioxolanes, containing a methoxy group in the 4 position.

2. It was shown that only the methyllactolides of tertiary α-oxo alcohols enter into the condensation. In the case of the methyllactolides of primary and secondary α-oxo alcohols the principal end reaction product is the corresponding α-oxo alcohol, which is formed in the decomposition of the intermediate complex of α-methoxy oxide with catalyst.

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SYNTHESIS OF AMINO ACID DERIVATIVES IN ADENOSINE-2'-PHOSPHORIC ACID SERIES

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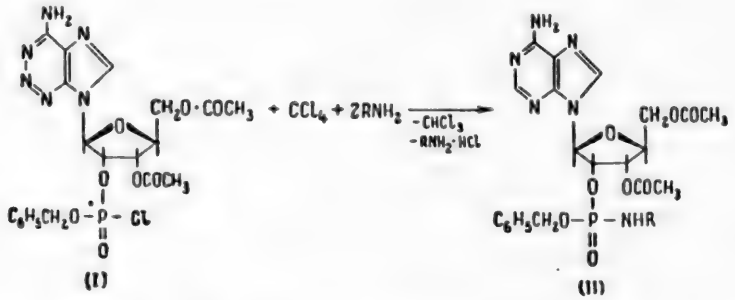
In our laboratory we recently synthesized a number of phosphoamino acid derivatives of muscle adenylic acid and investigated some of the properties of the obtained compounds [1]. The present paper is devoted to the synthesis of some phosphoamino acid derivatives in the adenosine-2'-phosphoric acid series.

It should be mentioned that the synthesis of nucleoside-2'-phosphoamides has not been described up to now. The main reason for this is the difficulty of forming the phosphoamido linkage in the nucleoside-2'-phosphate, as it has a free cis-hydroxyl group attached to the adjacent carbon atom (C_3'). This circumstance does not permit using, for example, the carbodiimide method, used successfully in the case of nucleoside-5'-phosphoamides [2], for the construction of the phosphoamido linkage, since treatment of the nucleoside-2'-phosphate (or nucleoside-3'-phosphate) with dicyclohexylcarbodiimide leads to the formation of the corresponding nucleoside-2',3'-cyclophosphate [3].

In this paper we accomplished the synthesis of adenosine-2'-phosphoamides (II) by reacting 3',5'-diacetyladenosine-2'-benzyl phosphite (I) [4] with the ester of the amino acid or peptide in the presence of carbon tetrachloride [5], according to the scheme:



(I) (II)

a) $R = CH_2COOC_2H_5$; b) $R = CH[CH(CH_3)_2]COOCH_3$; c) $R = CH(CH_2C_6H_5)COOCH_3$; d) $R = CH(CH_2C_6H_5)CONHCH_2COOCH_3$.

The synthesized compounds are colorless, amorphous, hydroscopic substances with low melting points. The structure of the obtained compounds follows from their mode of synthesis and is confirmed by the infrared and ultraviolet absorption spectra, and also by the results of acid and alkaline hydrolysis. The infrared absorption spectra indicate that the characteristic frequencies of the P=O and P-N linkages are present in the obtained compounds. The ultraviolet absorption spectra show that in the 200-300 mμ range the compounds exhibit one sharply

defined absorption maximum at 260 mμ, characteristic for the adenine group. Hydrolysis of the obtained compounds leads to the formation of the nucleotide (or the products of its further decomposition), on the one hand, and the amino acid (or peptide), on the other.

It should be mentioned that the obtained compounds are hydrolyzed with exceeding ease in alkaline medium, whereas their acid hydrolysis proceeds at a much slower rate. Thus, for example, the methyl ester of N-(3',5'-diacetyladenosine-2'-benzylphospho)-phenylalanine (IIc) is practically completely hydrolyzed in 1 min by 1N NaOH solution at 37°. A similar behavior is observed in the case of peptide derivative (IId) when it is hydrolyzed with either 1N or 0.1N NaOH solution. Treatment of the same compounds (IIc) and (IId) with 1N sulfuric acid solution fails to lead to their complete hydrolysis even 1.5 hr after the start of experiment.

In connection with such a sharp difference in the alkaline and acid hydrolysis rates of the obtained compounds it is important to mention the fact that O-acetyl groups are stable in acid, but are easily cleaved in alkaline medium [4, 6].

A comparison of these facts makes it possible to postulate that the high alkaline hydrolysis rate may be due to a rapid cleavage of the acetyl groups in alkaline medium and the formation of compounds with a free 3'-cis-hydroxyl group, which, in turn, creates the possibility of further hydrolysis of both the phosphoamido and the phospho ester linkage through the intermediate stage of forming the adenosine-2',3'-cyclophosphate structure.

The fact that the alkaline hydrolysis of adenosine-5'-phosphoamino acids (for which the formation of intermediate cyclophosphate structures is excluded) proceeds under comparable conditions at a much slower rate [7] is additional evidence in support of this postulation.

EXPERIMENTAL

Distributive chromatography on paper. The paper used for the chromatographic analysis was labeled "Chromatographic B", manufactured by the Volodar plant in Leningrad. The following systems of solvents were used: n-C_4H_9OH–H_2O–CH_3COOH (4 : 1 : 5) (top layer) (System 1); iso-C_3H_7OH–NH_4OH (d 0.884)–H_2O (7 : 1 : 2) (System 2); iso-$C_5H_{11}OH$–5% Na_2HPO_4 (both phases) (System 3). The compounds were detected on the chromatograms by ultraviolet absorption [8], and also by means of the molybdate [9] and benzidine [10] reagents. The compounds with a free α-amino group were developed using ninhydrin. The R_f values given below relate to ascending chromatograms. In the cases where the R_f values are not indicated, the compounds were identified on the chromatograms by direct comparison with authentic specimens.

3',5'-diacetyladenosine-2'-benzyl phosphite (I) was obtained by the phosphorylation of 3',5'-diacetyladenosine* with the mixed anhydride prepared from diphenylphosphoric and monobenzylphosphorous acids [4]. R_f 0.76 (System 1).

Ethyl ester of N-(3',5'-diacetyladenosine-2'-benzylphospho)-glycine (IIa). A solution of 0.05 g (0.0005 mole) of ethyl glycinate in 1 ml of dry CCl_4 was added to a solution of 0.07 g (0.00014 mole) of 3',5'-diacetyladenosine-2'-benzyl phosphite (I) in 1 ml of dry acetonitrile and 5 ml of dry CCl_4. The mixture was allowed to stand for 12 hr at 20°, after which it was evaporated in vacuo, the residue dissolved in 35 ml of chloroform, and the solution washed in succession with 5 ml of water, 5 ml of 0.05N hydrochloric acid, 5 ml of saturated aqueous sodium bicarbonate solution, and again with 5 ml of water; then the solution was dried over anhydrous sodium sulfate, evaporated in vacuo to a small volume, and treated with an excess of dry petroleum ether (b.p. 70-90°). The obtained colorless amorphous precipitate was separated, purified further by a double reprecipitation from chloroform with petroleum ether, and dried in a vacuum-desiccator over P_2O_5 and paraffin. Yield 0.04 g (49%). M.p. 35°. R_f 0.84 (System 1).

Ultraviolet absorption: λ_{max} 260 mμ; ϵ_{max} 13,900 (96% ethanol).

Infrared absorption: 1234 cm^{-1} (8.10μ) (frequency of P = O linkage [11]); 3340-3370 cm^{-1} (2.99-2.96μ) (frequency of the N-H linkage [11]); 867 cm^{-1} (11.53μ) (frequency of the P-N linkage [12]).

* 3',5'-Diacetyladenosine was isolated by counterflow extraction from the mixture of substances form in the acetylation of 5'-acetyladenosine [4].

We wish to thank M. G. Brazhnikova and R. N. Trofileeva for the help given us in carrying out the counterflow distribution. We also wish to thank V. M. Baikin and A. S. Khokhleva for their help in setting up the experimental counterflow distribution apparatus.

Found %: N 13.81; P 4.54. $C_{25}H_{31}O_{10}N_6P$. Calculated %: N 13.85; P 5.10.

Acid hydrolysis of (IIa). A solution of 5 mg of the substance in 0.2 ml of ethanol was treated with 0.4 ml of 0.1N sulfuric acid and the mixture wasallowed to stand at 37°. Samples were removed periodically, and were analyzed chromatographically in System 1. All of the samples, beginning with the 5-minute one and ending with the 4-hour sample, were found to contain, besides the starting compound (R_f 0.84), ethyl glycinate, glycine, and yeast adenylic acid.

The methyl ester of N-(3',5'-diacetyladenosine-2'-benzylphospho)-valine (IIb) was obtained in the same manner as the preceding from 0.07 g (0.00014 mole) of (I) and 0.05 g (0.0004 mole) of methyl valinate in the presence of dry CCl_4. Yield 0.03 g (38%). M.p. 77°. R_f 0.88 (System 1).

Ultraviolet absorption: λ_{max} 260 mμ; ϵ_{max} 13,510 (96% ethanol).

Infrared absorption: 1230 cm^{-1} (8.13 μ); 3350-3376 cm^{-1} (2.98-2.96 μ); 865 cm^{-1} (11.56 μ).

Found %: N 13.44; P 4.49. $C_{27}H_{35}O_{10}N_6P$. Calculated %: N 13.24; P 4.88.

Alkaline hydrolysis of (IIb). A solution of 5 mg of the substance in a mixture of 0.2 ml of ethanol and 0.5 ml of 0.1N NaOH solution was allowed tostand at 37°. Samples were removed at periodic intervals, and were analyzed chromatographically. Here a rapid disappearance of the starting compound was observedwith the appearance of valine, yeast adenylic acid and also adenosine in the hydrolyzate.

The methyl ester of N-(3',5'-diacetyladenosine-2'-benzylphospho)-phenylalanine (IIc) was obtained in the same manner as (IIa) from 0.1 g (0.0002 mole) of (I) and 0.53 g (0.003 mole) of the methyl ester of phenylalanine in the presence of dry CCl_4. Yield 0.11 g (85%). M.p. 73°. R_f 0.90 (System 1).

Ultraviolet absorption: λ_{max} 260 mμ; ϵ_{max} 13,100 (96% ethanol).

Infrared absorption: 1220 cm^{-1} (8.20 μ); 3335 cm^{-1} (3.00 μ); 867 cm^{-1} (11.53 μ).

Found %: C 54.37; H 5.49; N 12.32; P 5.08. $C_{31}H_{35}O_{10}N_6P$. Calculated %: C 54.54; H 5.17; N 12.31; P 4.53.

Acid hydrolysis of (IIc). A solution of 5 mg of the substance in a mixture of 0.2 ml of ethanol and 0.4 ml of 1N sulfuric acid was kept at 37° for 1.5 hours; samples were removed at periodic intervals and analyzed chromatographically in Systems 1 and 2. All of the samples, including the 90-minute one, contained the starting substance (R_f 0.90 in System 1); the hydrolyzate samples also contained yeast adenylic acid, the methyl ester of phenylalanine, and phenylalanine.

Alkaline hydrolysis of (IIc). A solution of 5 mg of the substance in a mixture of 0.2 ml of ethanol and 0.4 ml of 0.1N NaOH solution was allowed to stand in a thermostat at 37°. Samples were removed at periodic intervals, and were analyzed chromatographically in Systems 1 and 2. Beginning with the 1-minute sample, the starting substance was absent in all of the samples. The hydrolyzate samples were found to contain phenylalanine, yeast adenylic acid and adenosine.

The methyl ester of N-(3',5'-diacetyladenosine-2'-benzylphospho)-phenylalanylglycine (IId) was obtained in the same manner as (IIa) from 0.125 g (0.00024 mole) of (I) and 0.210 g (0.0009 mole) of the methyl ester of phenylalanylglycine* in the presence of dry CCl_4. Yield 0.130 g (71%). M.p. 108°. R_f 0.90 (System 1).

Ultraviolet absorption: λ_{max} 260 mμ; ϵ_{max} 12,180 (96% ethanol).

Infrared absorption: 1220-1230 cm^{-1} (8.20-8.13 μ); 864 cm^{-1} (11.57 μ).

The substance is very hydroscopic. For analysis it was dried for 7 days over P_2O_5 at 60° (5 mm).

Found %: C 52.55; H 5.81; N 12.78; P 3.53. $C_{33}H_{38}O_{11}N_7P \cdot H_2O$. Calculated %: C 52.31; H 5.32; N 12.94; P 4.08.

Acid hydrolysis of (IId). A solution of 5 mg of the substance in a mixture of 0.2 ml of ethanol and 0.5 ml of 1N sulfuric acid was kept for 2 hr at 37°. Samples were removed at periodic intervals and analyzed chromatographically in Systems 1, 2, and 3. All of the samples, including the 120-minute one, were found to contain the starting substance (IId). The hydrolyzate samples were also found to contain phenylalanine, yeast adenylic acid, and traces of adenosine.

* The methyl ester of phenylalanylglycine was obtained by the catalytic hydrogenation of its carbobenzoxy derivatives [13].

Alkaline hydrolysis of (IId). a) A solution of 5 mg of the substance in 0.2 ml of ethanol and 0.5 ml of 1N NaOH solution was kept in a thermostat at 37°. Samples were removed at periodic intervals and analyzed chromatographically in Systems 1, 2, and 3. Beginning with the 1-minute sample, the starting substance (IId) was absent in all of the samples. The hydrolyzate samples were found to contain phenylalanylglycine, yeast adenylic acid and adenosine.

b) Operating in the same manner as described above, 5 mg of the substance was hydrolyzed using 0.1N NaOH solution. Beginning with the 1-minute sample, here the starting substance (IId) was also absent in all of the samples.

SUMMARY

1. The synthesis of amino acid derivatives in the adenosine-2'-phosphoric acid series with a phosphoamide type of linkage was accomplished. The ethyl ester of N-(3',5'-diacetyl-adenosine-2'-benzylphospho)-glycine, the methyl ester of N-(3',5'-diacetyladenosine-2'-benzylphospho)-valine, the methyl ester of N-(3',5'-diacetyl-adenosine-2'-benzylphospho)-phenylalanine and the methyl ester of N-(3',5'-diacetyladenosine-2'-benzylphospho)-phenylalanylglycine were obtained.

2. The structure of the obtained compounds follows from the mode of synthesis and is supported by the infrared and ultraviolet absorption spectra, and also by the results of acid and alkaline hydrolysis.

3. It was established that the synthesized compounds are hydrolyzed slowly by acid, but are cleaved very rapidly in alkaline medium. A theory was expressed regarding the mechanism of the alkaline hydrolysis.

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RESEARCH IN THE FIELD OF THE REACTION OF C-ACYLATION OF HETEROCYCLIC KETO-ENOLS

II. SYNTHESIS OF α-ACETYL- AND α-PROPIONYL-γ-PHENYLTETRONIC ACIDS

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α-Acetyl-γ-phenyltetronic acid was obtained for the first time by the interaction of α-bromophenylacetyl bromide with the ethyl ester of β-aminocrotonic acid with subsequent hydrolysis of the α-imonoacetyl-γ-phenyltetronic acid, the yield of the final product not being indicated [1]. Later, α-acetyl-γ-phenyltetronic acid was obtained with 54.5% yield by acetoacetylation of methyl mandelate by means of diketene with subsequent cyclization of the methyl-O-acetoacetylandelate which was obtained as an intermediate [2].

The preparation of α-acetyl derivatives of γ-substituted tetronic acids has been accomplished by Friedel-Crafts acetylation of the corresponding tetronic acids and by a Fries rearrangement of O-acetyltetronic acids [3]. However, the α-acetyl-γ-phenyltetronic acid which was obtained with 20% yield in the Friedel-Crafts reaction was subjected to five crystallizations in its purification, and the product obtained by the Fries rearrangement required paper chromatography ten times.

There is no information in the literature on other α-acyl-γ-phenyltetronic acids.

Continuing the studies on the C-acylation of heterocyclic keto-enols [4] by means of aliphatic acids, we carried out the synthesis of α-acetyl- and α-propionyl-γ-phenyltetronic acid by the acylation of γ-phenyltetronic acid with the corresponding acids in a polyphosphoric acid medium. We obtained the α-acyl-γ-phenyltetronic acids with 50-60% yields, which permits consideration of this method of their synthesis as the most favorable from the preparative point of view.

For identification, we also prepared α-acetyl-γ-phenyltetronic acid from O-acetylmandelyl chloride and sodioacetoacetic ester, by analogy with 3-acetyl-4-hydroxycoumarin [5].

EXPERIMENTAL

γ-Phenyltetronic Acid was synthesized by the Anschutz method by saponification (with simultaneous decarboxylation) of α-carbethoxy-γ-phenyltetronic acid, which was prepared from O-acetylmandelyl chloride and sodiomalonic ester. M.p. 127-128° (according to literature data, m.p. 127.5-128.5° [6]).

α-Acetyl-γ-phenyltetronic Acid. A mixture of 2 g of γ-phenyltetronic acid, 10 ml of glacial CH_3COOH, and 60 g of polyphosphoric acid (prepared from 100 g of P_2O_5 and 64 ml of 85% H_3PO_4 [7]) was heated in a water bath for 3 hours with stirring. The resulting solution was poured while hot onto ice; on the following day the precipitate was filtered off, washed with water, and dried at 50-60°. Yield of α-acetyl-γ-phenyltetronic acid 1.3 g (52.4%), m.p. 98-101°. After recrystallization from petroleum ether – colorless plates with m.p. 102-103.5° (according to literature data, m.p. 104° [1]).

α-Propionyl-γ-phenyltetronic Acid. This compound was obtained analogously, starting with 2 g of γ-phenyltetronic acid, 12.5 ml of C_2H_5COOH, and 60 g of polyphosphoric acid; yield 1.58 g (59.9%). After recrystallization from petroleum ether – slightly yellowish needles with m.p. 81-82.5°.

Found %: C 67.35, 67.46; H 5.11, 4.92. $C_{13}H_{12}O_4$. Calculated %: C 67.23; H 5.20.

Preparation of α-Acetyl-γ-phenyltetronic Acid from O-Acetylmandelyl Chloride. To a suspension of sodioacetoacetic ester (9.1 g of freshly distilled acetoacetic ester and 1.61 g of Na) in 75 ml of anhydrous benzene, a solution of 5 g of O-acetylmandelyl chloride [6] in 10 ml of anhydrous benzene was added dropwise with cooling. The reaction mixture was refluxed with stirring for 10 hours, and the orange-colored precipitate was filtered off, washed with anhydrous ether, dried in air, dissolved in 15 ml of water, and filtered off from the water-insoluble residue. The filtrate was extracted with ether, the aqueous layer was acidified with concentrated hydrochloric acid (with cooling), and the white-colored precipitate was filtered off, washed with water, and air-dried. Yield of α-acetyl-γ-phenyltetronic acid 0.7 g (13.6%), m.p. 102-103°. A mixed sample of this substance with that obtained by the above-described method did not give any melting-point depression.

SUMMARY

A new method has been developed for the preparation of α-acetyl- and α-propionyl-γ-phenyltetronic acid by acylation of γ-phenyltetronic acid by the respective carboxylic acids in the presence of polyphosphoric acid.

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N-CARBETHOXYHYDROPYRIDAZINES AND THEIR DERIVATIVES

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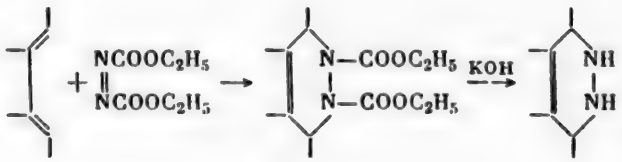
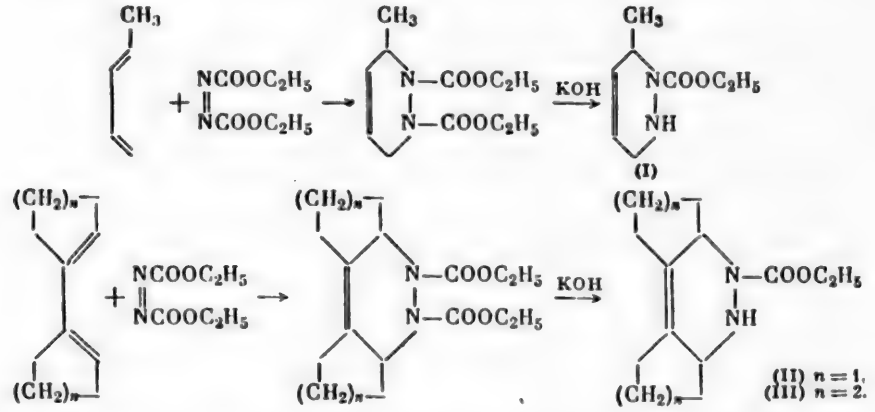
The alkaline hydrolysis of adducts of azodicarboxylic ester with dienes leads to the formation of tetrahydropyridazines [1-5].

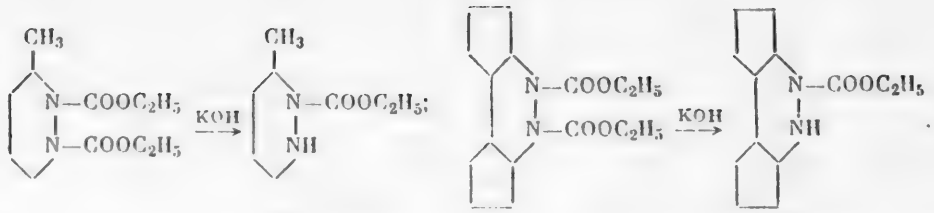


Under certain conditions (smaller quantity of alkali) partial hydrolysis of the adducts can be accomplished, leading to the formation of N-carbethoxy-Δ^4-tetrahydropyridazines [2, 5].

In the present work, by partial hydrolysis of the adducts of azodicarboxylic ester with piperylene, 1,1'-dicyclopentenyl, and 1,1'-dicyclohexenyl, the corresponding N-carbethoxy compounds (I-III) were obtained.



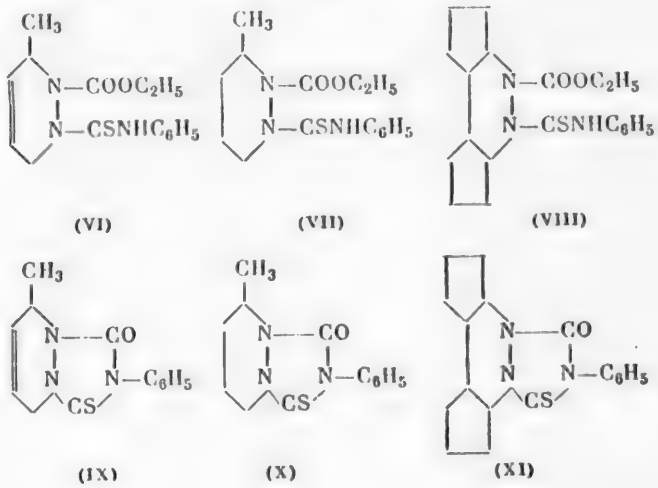
In like manner – by partial hydrolysis of the hydrogenated adducts – the N-carbethoxyhexahydropyridazines (IV, V) were obtained.



(IV) (V)

Earlier, in [2], we had demonstrated the fact that the carbethoxy group is retained on the nitrogen atom nearest to the substituent in the instance of hydrolysis of adducts of azodicarboxylic ester with tolylbutadienes.

The liquid N-carbethoxyhydropyridazines (I, IV, V) were characterized by their addition products with phenyl isothiocyanate. It was established that the thus-formed substituted phenylthioureas (anilides of 2-carbethoxyhydropyridazine-1-thiocarboxylic acids, VI-VIII) upon heating readily lose a molecule of alcohol with the formation of the bicyclic system of sym-triazolidino-(1, 2-1,2)-hydropyridazine (IX-XI).



(VI) (VII) (VIII)

(IX) (X) (XI)

EXPERIMENTAL

N-Carbethoxy-Δ^4-tetrahydro- and hexahydropyridazines were obtained by partial hydrolysis of 1,2-dicarbethoxy-Δ^4-tetrahydro- and hexahydropyridazines (adducts of azodicarboxylic ester with dienes, and their dihydrides). The hydrolysis was carried out by 4-hour steam-bath heating of a solution of 0.2 mole of the dicarbethoxy compound and 28 g of potassium hydroxide in 150 ml of alcohol. The precipitated potassium carbonate was removed by vacuum filtration and washed on the filter with ether. The solvents were distilled from the filtrate and the reaction product was separated from the residue by vacuum distillation. In the case of the adducts of azodicarboxylic ester with 1,1'-dicyclopentenyl and 1,1'-dicyclohexenyl, the reaction products had crystallized after distilling off the ether, and their purification was accomplished by recrystallization from a mixture of alcohol and 90-95° petroleum ether. The constants, yields, and analytical data on the carbethoxy compounds (I-V) thus obtained are presented in Table 1.

Addition of N-Carbethoxy Compounds to Phenyl Isothiocyanate was accomplished by heating a mixture of the reactants (slight excess of phenyl isothiocyanate) for 5-10 minutes at 60-80°. The reaction product was washed with 50% alcohol and with petroleum ether and recrystallized from a 1:1 mixture of alcohol and 90-95° petroleum ether. The constants and analytical data on the substituted phenylthioureas which were obtained (anilides of 2-carbethoxyhydropyridazine-1-thiocarboxylic acids; VI-VIII) are presented in Table 2.

Cyclization of these compounds was accomplished by heating them at 150-180° for 5-10 minutes. The cyclic reaction products, derivatives of sym-triazolidino-(1,2-1,2)-hydropyridazines (IX-XI), were recrystallized from alcohol; their constants and analytical data are presented in Table 2.

TABLE 1

N-Carbethoxytetra- and Hexahydropyridazines

Formula No.	Name	Yield (%)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found (%) C	Found (%) H	Found (%) N	Empirical formula	Calculated (%) C	Calculated (%) H	Calculated (%) N
(I)	3-Methyl-2-carbethoxy-Δ^4-tetrahydropyridazine	52	110° (9)	1.4840	1.0817	45.00	45.29	56.40, 56.48	8.30, 8.41	—	$C_8H_{14}O_2N_2$	56.45	8.29	—
(II)	3,4,5,6-bis-Cyclopentano-1-carbethoxy-Δ^4-tetrahydropyridazine	45	167—168•• (8)	—	—	—	—	66.15, 66.32	8.68, 6.73	—	$C_{13}H_{20}O_2N_2$	66.07	8.53	—
(III)	3,4,5,6-bis-Cyclohexano-1-carbethoxy-Δ^4-tetrahydropyridazine	78	179—180••• (8)	—	—	—	—	67.96, 68.04	9.15, 9.34	10.78, 10.75	$C_{15}H_{24}O_2N_2$	68.14	9.15	10.60
(IV)	3-Methyl-2-carbethoxyhexahydropyridazine	60	105—107 (7)	1.4646	1.0405	45.67	45.76	55.60, 55.74	9.30, 9.45	16.00, 16.11	$C_8H_{16}O_2N_2$	55.79	9.36	16.27
(V)	3,4,5,6-bis-Cyclopentano-1-carbethoxyhexahydropyridazine	43	170—173 (10)	1.5090	1.1042	64.46	64.45	65.32, 65.42	9.34, 9.40	12.04, 12.02	$C_{13}H_{22}O_2N_2$	65.51	9.30	11.76

• Atomic refraction of nitrogen taken equal to 2.48 [6].

•• M.p. 62.5-63°.

••• M.p. 84.5-85°.

TABLE 2

Anilides of 2-Carbethoxyhydropyridazine-1-Thiocarboxylic Acids and Products of Their Cyclization, sym-Triazolidino-(1,2-1,2)-Hydropyridazines

Formula No.	Name	Melting point	Found (%)			Empirical formula	Calculated (%)		
			C	H	N		C	H	N
(VI)	Anilide of 3-methyl-2-carbethoxy-Δ^4-tetrahydropyridazine-1-thiocarboxylic acid	183°	59.25, 59.15	6.31, 6.23	••	$C_{15}H_{19}O_2N_3S$	58.98	6.27	
(VII)	Anilide of 3-methyl-2-carbethoxyhexahydropyridazine-1-thiocarboxylic acid	119—120•	58.81, 58.71	6.75, 6.84	13.60, 13.52	$C_{15}H_{21}O_2N_3S$	58.60	6.89	13.67
(VIII)	Anilide of 3,4,5,6-bis-cyclopentano-2-carbethoxyhexahydropyridazine-1-thiocarboxylic acid	124—126•	64.54, 64.57	7.51, 7.51	11.04, 11.25	$C_{20}H_{27}O_2N_3S$	64.31	7.29	11.25
(IX)	Cyclization product from (VI)	177—178	60.21, 60.30	5.16, 5.17	16.09, 16.21	$C_{12}H_{13}ON_3S$	60.21	5.05	16.20
(X)	Cyclization product from (VII)	138—139	59.70, 59.65	5.69, 5.60	15.98, 16.03	$C_{13}H_{15}ON_3S$	59.74	5.79	16.08
(XI)	Cyclization product from (VIII)	145—145.5	66.22, 66.12	6.46, 6.45	•••	$C_{18}H_{21}ON_3S$	66.02	6.47	

• With rapid heating; melted with decomposition.

•• Found %: S 10.10, 10.25. Calculated %: S 10.50.

••• Found %: S 9.65, 9.63. Calculated %: S 9.79.

SUMMARY

1. By partial hydrolysis of the adducts of azodicarboxylic ester with piperylene, dicyclopentenyl, and dicyclohexenyl, the corresponding N-carbethoxy-Δ^4-tetrahydropyridazines have been obtained.

2. N-Carbethoxyhexahydropyridazines have been obtained analogously from the hydrogenated adducts of azodicarboxylic acid with piperylene and dicyclopentenyl.

3. It has been established that when the N-carbethoxyhydropyridazines which were obtained are added to phenyl isothiocyanate, the addition products are readily cyclized, forming the sym-triazolidino-(1,2-1,2)-hydropyridazine system.

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TETRAHYDROPYRIDAZINES AND HEXAHYDROPYRIDAZINES

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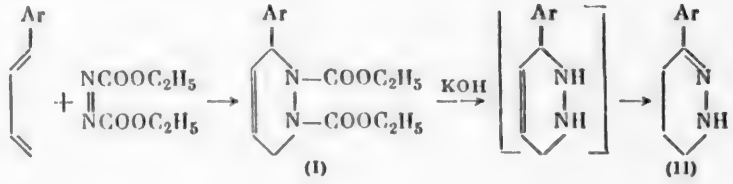
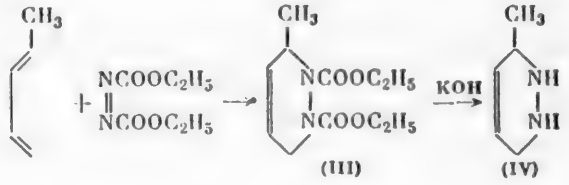
In previous communications we described a new method of synthesizing arylcyclobutanes by catalytic decomposition of aryltetrahydropyridazines [1-3]. In connection with further study of the possibility of synthesizing alkylcyclobutanes and cycloalkanocyclobutanes by this same method [4], it was necessary to synthesize the corresponding tetrahydropyridazines with a different position of the double bond.

The simplest method of preparing tetrahydropyridazines is the hydrolysis and decarboxylation of adducts of azodicarboxylic ester with dienes. It is known that adducts of arylbutadienes (I) upon hydrolysis give simultaneous decarboxylation and a shift of the double bond from position 4 to position 2, resulting in the formation of aryl-Δ^2-tetrahydropyridazines (II) [1-3, 5].



(I) (II)

In the present work it is shown that the adduct of piperylene with azodicarboxylic ester (III) upon hydrolysis does not show the double-bond shift; 3-methyl-Δ^4-tetrahydropyridazine (IV) is obtained.

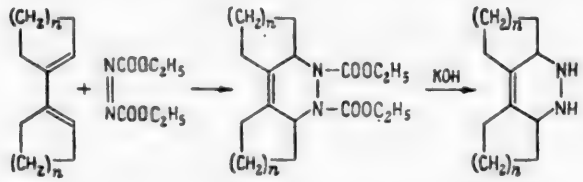


(III) (IV)

The 3-methyltetrahydropyridazine obtained by this method gives a dibenzoyl derivative which is identical with the 3-methyl-1,2-dibenzoyl-Δ^4-tetrahydropyridazine synthesized by the interaction of azodibenzoyl with piperylene [6] (mixed sample did not give any melting-point depression). The absorption spectrum of 3-methyl-Δ^4-tetrahydropyridazine in the infrared region contains a broad band at 3212-3306 cm^{-1}, corresponding to two NH groups• [7].

• A similar broad band at 3296-3316 cm^{-1} is also observed in the infrared spectrum of 3-methylhexahydropyridazine.

Similarly, the adducts of azodicarboxylic ester with 1,1'-dicyclopentenyl (V) and 1,1'-dicyclohexenyl (VII) upon hydrolysis gave the corresponding bis-cycloalkano-Δ^4- tetrahydropyridazines (VI) and (VIII).

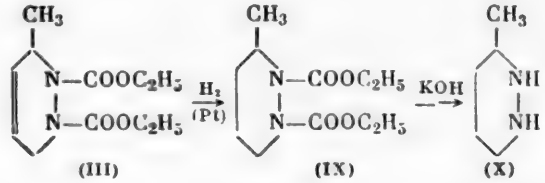


(V) $n=1$, (VI) $n=1$,
(VII) $n=2$, (VIII) $n=2$.

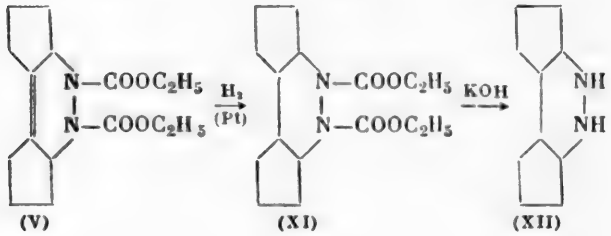
The dibenzoyl derivative of the bis-cyclopentano-Δ^4-tetrahydropyridazine is identical with the bis-cyclopentano-1,2-dibenzoyl-Δ^4-tetrahydropyridazine obtained by the diene synthesis from azodibenzoyl and 1,1'-dicyclopentenyl [6].

Thus, in the hydrolysis of adducts of azodicarboxylic ester with the alkylbutadiene or with the bis-cycloalkanobutadienes (in contrast with the hydrolysis of adducts with arylbutadienes) the shift of the double bond to the nitrogen atom does not occur.

An indirect method was utilized for the purpose of preparing alkyl- and bis-cycloalkanotetrahydropyridazines with the double bond at the nitrogen atom. Hydrogenated adducts of piperylene and 1,1'-dicyclopentenyl* with azodicarboxylic ester were hydrolyzed to obtain the corresponding hexahydropyridazines.

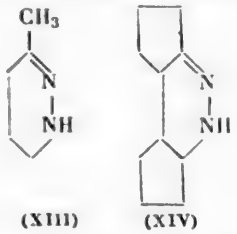


(III) (IX) (X)



(V) (XI) (XII)

The hexahydropyridazines (X) and (XII) were then subjected to oxidation, using as oxidizers hydrogen peroxide (with traces of cupric chloride), mercuric oxide, and ammoniacal cupric hydroxide solution. It was found that in the process of oxidation there also occurs a shift of the double bond to position 2, giving the Δ^2-tetrahydropyridazines (XIII) and (XIV) in place of the expected Δ^1-tetrahydropyridazines.



(XIII) (XIV)

* The adduct of azodicarboxylic ester with 1,1'-dicyclohexenyl could not be hydrogenated successfully in the presence of platinum and palladium even at 75°.

TABLE 1

Δ^4-Tetrahydropyridazines and Their Derivatives

Name	Yield (%)	Melting point (from alcohol)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.*	Found (%) C	Found (%) H	Found (%) N	Empirical formula	Calculated (%) C	Calculated (%) H	Calculated (%) N
3-Methyl-1,2-dicarbethoxy-Δ^4-tetrahydropyridazine** (III)	86	—	146° (8)	1.4684	1.1171	60.33	60.79	—	—	—	$C_{11}H_{18}O_4N_2$	—	—	—
3-Methyl-Δ^4-tetrahydropyridazine (IV)	63	—	63 (15)	1.4950	0.9735	29.40	29.78	—	—	—	$C_5H_{10}N_2$	—	—	—
Dibenzoyl derivative of (IV)****	—	121.5—122°	—	—	—	—	—	74.60, 74.51	5.70, 5.82	9.12, 9.05	$C_{19}H_{18}O_2N_2$	74.49	5.92	9.14
Phenylthiourea from (IV)	—	112.5—113	—	—	—	—	—	62.02, 61.81	6.61, 6.60	17.97, 18.16	$C_{12}H_{15}N_3S$	61.77	6.48	18.01
3,4,5,6-bis-Cyclopentano-1,2-dicarbethoxy-Δ^4-tetrahydropyridazine (V)	78	53—54***	207—208 (12)	1.5073 supercooled	—	—	—	62.27, 62.16	7.97, 7.87	—	$C_{16}H_{24}O_4N_2$	62.31	7.85	—

* Atomic refraction of nitrogen taken equal to 2.48 [10].

** Literature data [11]: B.p. 118° (0.5 mm), n_D^{18} 1.4704, d_{18}^{18} 1.115.

*** From petroleum ether.

**** Literature data [6]: M.p. 121-122°; obtained from piperylene and azodibenzoyl.

TABLE 1 (Continued)

Name	Yield (%)	Melting point (from alcohol)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found (%) C	Found (%) H	Found (%) N	Empirical formula	Calculated (%) C	Calculated (%) H	Calculated (%) N
3,4,5,6-bis-Cyclopentano-Δ^4-tetrahydropyridazine (VI)	28	—	132—135 (10)*****	—	—	—	—	—	—	—	—	—	—	—
Dibenzoyl derivative of (VI)**	—	201—202	—	—	—	—	—	77.30, 77.33	6.40, 6.34	7.52, 7.69	$C_{24}H_{24}O_2N_2$	77.39	6.50	7.52
Phenylthiourea from (VI)	—	128	—	—	—	—	—	68.43, 68.23	7.15, 7.13	10.21, 10.58	$C_{17}H_{21}N_3S$	68.19	7.07	10.71
3,4,5,6-bis-Cyclohexano-1,2-dicarbethoxy-Δ^4-tetrahydropyridazine (VII)	75	42—43	205—206 (8)	1.5080 supercooled	—	—	—	64.21, 64.18	8.30, 8.41	—	$C_{18}H_{28}O_4N_2$	64.26	8.39	—
3,4,5,6-bis-Cyclohexano-Δ^4-tetrahydropyridazine (VII)	54	45—46	—	—	—	—	—	—	—	—	—	—	—	—
Dibenzoyl derivative of (VIII)	—	188—189	—	—	—	—	—	77.90, 77.83	7.00, 7.09	—	$C_{26}H_{28}O_2N_2$	77.97	7.05	
Phenylthiourea from (VIII)	—	205—206	—	—	—	—	—	69.71, 69.91	7.87, 7.90	—	$C_{19}H_{25}N_3S$	68.68	7.69	7.79

* The substance decomposed upon distillation; yield is indicated on the distilled substance.

** Literature data [6]: M.p. 201-202°; obtained from 1,1'-dicyclopentenyl and azodibenzoyl.

TABLE 2

Hexahydropyridazines and Their Derivatives

Name	Yield (%)	Melting point (from alcohol)	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.*	Found (%) C	Found (%) H	Found (%) N	Empirical formula	Calculated (%) C	Calculated (%) H	Calculated (%) N
3-Methyl-1,2-dicarbethoxyhexahydropyridazine** (IX)	95	—	155–156° (12)	1.4623	1.0982	61.17	61.27	—	—	—	$C_{11}H_{20}O_4N_2$	—	—	—
3-Methylhexahydropyridazine (X)	87	—	73 (29) 45–46 (8)	1.4742	0.9350	30.12	30.25	—	—	—	$C_5H_{12}N_2$	—	—	—
Dibenzoyl derivative of (X)	—	132–133°	—	—	—	—	—	73.81, 74.02	6.66, 6.74	—	$C_{19}H_{20}O_2N_2$	74.00	6.54	9.08
bis-Phenylthiourea from (X)	—	163–163.5	—	—	—	—	—	61.59, 61.46	5.82, 5.80	—	$C_{19}H_{22}N_4S_2$	61.59	5.98	—
3,4,5,6-bis-Cyclopentano-1,2-dicarbethoxyhexahydropyridazine (XI)	93	—	187–188 (4)	1.4957	1.1372	79.69	79.96	62.02, 61.90	8.60, 8.58	8.95, 8.87	$C_{16}H_{26}O_4N_2$	61.91	8.44	9.03
3,4,5,6-bis-Cyclopentanohexahydropyridazine (XII)	77	—	141 (10)	1.5290	1.0623	48.17	48.24	—	—	—	$C_{10}H_{18}N_2$	—	—	—
Dibenzoyl derivative of (XII)	—	190.5–191	—	—	—	—	—	77.09, 77.15	7.11, 7.14	7.53, 7.37	$C_{24}H_{26}O_2N_2$	76.97	7.00	7.48
Phenylthiourea from (XII)	—	137–137.5	—	—	—	—	—	67.61, 67.64	7.75, 7.68	13.83, 13.77	$C_{17}H_{23}N_3S$	67.73	7.69	13.96

* Atomic refraction of nitrogen taken equal to 2.48 [10].

** Literature data [11]: B.p. 165° (25 mm), 128-129° (0.9 mm), n_D^{24} 1.4619.

TABLE 3

Δ^2-Tetrahydropyridazines and Their Derivatives

Name	Yield (%)	Melting point	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.*	Found (%) C	Found (%) H	Found (%) N	Empirical formula	Calculated (%) C	Calculated (%) H	Calculated (%) N
3-Methyl-Δ^2-tetrahydropyridazine (XIII)	82	—	65° (16)	1.4880	0.9666	29.27	29.20	—	—	—	$C_5H_{10}N_2$	—	—	—
Phenylthiourea from (XIII)	—	106°	—	—	—	—	—	65.60, 65.57	6.70, 6.78	12.60, 12.70	$C_{12}H_{15}N_3S$	65.71	6.89	12.78
3,4,5,6-bis-Cyclopentano-Δ^2-tetrahydropyridazine (XIV)	67	—	121—122° (8)	1.5310	1.0592	47.98	47.65	—	—	—	$C_{10}H_{16}N_2$	—	—	—
Phenylthiourea from (XIV)	—	149—150	—	—	—	—	—	67.99, 68.00	7.07, 6.96	13.99, 14.03	$C_{17}H_{21}N_3S$	68.19	7.07	14.04

* Increment of molecular refraction for > N-N = group taken equal to 5.87 [13].

The occurrence of this shift is verified by the fact that the tetrahydropyridazines obtained by such a method react with phenyl isothiocyanate, forming addition products. The infrared spectrum of 3-methyl-Δ^2-tetrahydropyridazine contains a narrow line at 3338 cm^{-1}, corresponding to the NH group [7]. A similar shift of the double bond – transition from the azo-form (Δ^1) to the hydrazono-form (Δ^2) – is known for diphenyl-Δ^1-tetrahydropyridazine [5], pyrazolines [8], and certain azo compounds [9].

It is interesting to note that all of the Δ^4-tetrahydropyridazines and hexahydropyridazines which we obtained (excluding the 3-methylhexahydropyridazine), although containing two NH groups and giving dibenzoyl derivatives, react with only one molecule of phenyl isothiocyanate, which may be explained by steric hindrances which prevent the addition of a second molecule of this reagent. Thus, the reaction with phenyl isothiocyanate can readily lead to a mistake in determining the position of the double bond (based on the number of NH groups) in tetrahydropyridazines.

EXPERIMENTAL

1,2-Dicarbethoxy-Δ^4-tetrahydropyridazines (the adducts of azodicarboxylic ester with piperylene, 1,1'-dicyclopentenyl, and 1,1'-dicyclohexenyl) were prepared by mixing benzene solutions of equimolar quantities of the reactants [10] and separated by vacuum distillation. The yields, constants, and analytical data are presented in Table 1.

Δ^4-Tetrahydropyridazines were prepared by 3-hour steam-bath heating of a solution of 0.2 mole of the adduct and 56 g (1 mole) of potassium hydroxide in 250 ml of alcohol. The precipitated potassium carbonate was separated and washed several times with ether. The solvent was removed from the filtrate by distillation, and the reaction product was separated from the residue either by vacuum distillation (in the case of 3-methyl-Δ^4-tetrahydropyridazine) or by extraction with benzene. The Δ^4-tetrahydropyridazines were characterized by dibenzoyl derivatives (prepared by a method described for the benzoylation of pyrazolines [12]) and by their addition products with phenyl isothiocyanate. The constants of the compounds which were obtained are presented in Table 1.

1,2-Dicarbethoxyhexahydropyridazines were obtained by hydrogenation of the adducts of azodicarboxylic ester with dienes (piperylene and 1,1'-dicyclopentenyl) in 30% alcoholic solution in the presence of platinum catalyst at 20-50°. The hydrogenated products were separated by vacuum distillation (see Table 2).

Hexahydropyridazines were obtained by hydrolysis of the hydrogenated adducts under the conditions indicated

above for hydrolysis of the adducts themselves. The reaction products were separated by vacuum distillation and were characterized by preparing dibenzoyl derivatives and addition products with phenyl isothiocyanate (see Table 2).

Δ^2-Tetrahydropyridazines were prepared by oxidation of hexahydropyridazines by three methods, which give almost identical yield. a) Cooling with ice and stirring, 15 ml of 30% perhydrol was added dropwise to a mixture of 0.1 mole of the hexahydropyridazine and a solution of 0.05 g of cupric chloride in 40 ml of water. The reaction product was extracted with ether, the ether extract was dried with potassium carbonate, and the Δ^2-tetrahydropyridazine was separated (after distilling off the ether) by vacuum distillation. b) Cooling with ice and stirring, 27 g (0.125 mole) of yellow mercuric oxide was added gradually to a solution of 1.0 mole of the hexahydropyridazine in 40 ml of anhydrous benzene or ether.

After adding all of the mercuric oxide, the mixture was stirred for 20 minutes at room temperature, the solution was decanted from the residue of metallic mercury and excess mercuric oxide, the solvent was distilled off, and the reaction product was separated by vacuum distillation. c) To a well-cooled solution of 0.1 mole of the hexahydropyridazine in 50 ml of water, there was added slowly with stirring a cold mixture of 100 ml of 25% ammonia solution with a solution of 51 g (0.3 mole) of cupric chloride in 70 ml of water. The reaction product was extracted with ether and separated in the usual manner. The constants, yields, and analytical data of the Δ^2-tetrahydropyridazines which were obtained and their addition products with phenyl isothiocyanate are presented in Table 3.

SUMMARY

1. It has been shown that in the hydrolysis of adducts of azodicarboxylic ester with alkyl- and cycloalkanobutadienes there is no shift of the double bond to the nitrogen atom, and Δ^4-tetrahydropyridazines are formed.

2. It has been established that upon oxidation of hexahydropyridazines, as a result of shifting the double bond, Δ^2-tetrahydropyridazines are formed.

3. It has been found that phenyl isothiocyanate in the majority of cases reacts with only one of the two adjacent NH groups of the Δ^4-tetrahydro- or hexahydropyridazine ring.

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INVESTIGATIONS IN THE FIELD OF POLYMETHYLENE RINGS

XXXV. SYNTHESIS OF CYCLOHEXANEDIONE-1,2 AND HEXANEDIONE-2,3 DIHYDRAZONES

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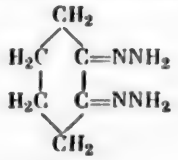
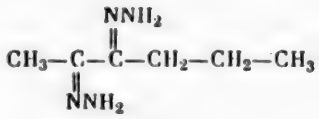
The synthesis of cyclohexanedione-1,2 dihydrazone (I) was investigated for the first time by Domnin and Glebovskaya [1]. Unfortunately these authors did not succeed in developing a satisfactory method for synthesizing the compound. Dihydrazone (I) was prepared only once and was not fully characterized.

We undertook to develop a method for synthesizing cyclohexanedione-1,2 dihydrazone (I). For comparison we planned also to synthesize the acyclic hexanedione-2, 3 dihydrazone (II).



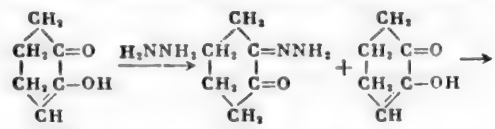
(I)



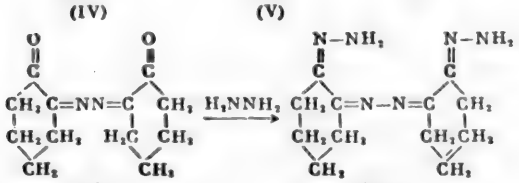
(II)

Variation of the conditions of synthesis, described earlier [1], proved to be inexpedient for the most part. The reaction conditions were varied by working with and without solvent and using water, a water-alcohol mixture, and anhydrous alcohol as solvents. Hydrazine hydrate or anhydrous hydrazine, depending on the aqueous or anhydrous solvent used, was added, but on addition of hydrazine to cyclohexanedione-1,2 the reaction product was always an orange oil which could not be crystallized. This oil was kept for several months, after which it was found to contain a small amount of crystals, which were separated from the oil, recrystallized, and characterized as cyclohexanedione-1,2 ketazine dihydrazone (III). In one case only, large crystals of cyclohexanedione-1,2 dihydrazone (I) separated out, as was described earlier [1]. Ketazine dihydrazone (III) was characterized by elementary analysis and by preparing a derivative with phthalic anhydride. On treatment with picric acid, ketazine dihydrazone (III) decomposed, hydrazine picrate being formed.

The formation of cyclohexanedione-1,2 ketazine dihydrazone (III) probably takes place according to the following scheme:



(IV) (V)



(VI) (III)

Cyclohexanedione-1,2 (IV) exists in the enol form [2]. The structures of the other intermediate products are unknown, since they were not isolated. It should be noted that on addition of hydrazine to diketone (IV) a precipitate formed – probably monohydrazone (V) – which could not be investigated owing to its instability. The presence of an excess of diketone (IV) in the initial reaction period favors the formation of monohydrazone (V), ketazine (VI), and polymeric chain ketazines. The formation of dihydrazone (I) under these conditions is unlikely, and indeed, it was isolated only in one experiment.

Proceeding from these considerations, we changed the order of addition of the reagents and obtained good yields of dihydrazone (I). We found, however, that it was difficult to crystallize the latter from the reaction mixture. Since examination of a model of dihydrazone (I) showed that steric hindrances to the formation of the latter do not exist, it must be presumed that the nonoccurrence of crystallization is due to the difficulty of nucleus formation. The reaction mixture is a supersaturated solution of dihydrazone (I) in alcohol, water, and hydrazine. Dihydrazone (I) is very soluble in these solvents, and crystals cannot form. Crystallization was accomplished only by priming. It should be noted that on recrystallization from dry benzene, dihydrazone (I) separated out without difficulty.

The structure of cyclohexanedione-1,2 dihydrazone (I) was confirmed by full elementary analysis and by molecular weight determination. Examination of the infrared spectrum confirmed the presence of a primary amino group (wavelengths 3340, 3175, 2960 cm^{-1}). It was very difficult to interpret the spectrum for lower wave numbers, since an emulsion of crystalline dihydrazone (I) in vaseline gave a spectrum with very low band intensity. Dihydrazone (I) is difficultly soluble in CCl_4, which made it impossible to obtain the spectrum of this substance in solution. On the basis of the records obtained, the presence in dihydrazone (I) of the C = N bond, whose intensity in the infrared spectrum is low, cannot be determined; however, it may be asserted with full confidence that compound (I) does not contain a keto group.

In order to compare properties and to determine whether the difficulty in preparing cyclohexanedione-1,2 dihydrazone (I) is due to steric hindrance, we synthesized hexanedione-2,3 dihydrazone (II). We attempted to synthesize the latter by the cited method [3] – oxidation of hexanone-2 to hexanedione-2,3 with selenium dioxide. However, this method proved unsuitable for synthesis of the diketone, since the reaction gave a low yield, and the boiling points of hexanone-2 (127°) and hexanedione-2,3 (128.9°) are very close, so that it proved impossible to separate them by fractional distillation.

Hexanedione-2,3 was prepared by a modified procedure [4] – oxidation of hexanone-2 with nitric acid. To perform the oxidation successfully, the conditions must be carefully chosen, since, if the conditions are too severe, the diketone is oxidized further, acids being formed. We isolated hexanedione-2,3 from the reaction mixture in the form of the free diketone, from which the dioxime was obtained. The latter was wholly identical in properties with the compound described in [4].

We prepared hexanedione-2,3 dihydrazone (II) by the method developed for cyclohexanedione-1,2 dihydrazone (I). It crystallizes from the reaction mixture without difficulty. Dihydrazone (II) was characterized by full elementary analysis and the molecular weight. The infrared spectrum showed the presence of a primary amino group (wave numbers: 3355, 3191, 2976 cm^{-1}) and the absence of a keto group. On interpreting the spectrum we encountered the same difficulties as with the spectrum of dihydrazone (I). The chemical behavior of dihydrazone (II) was investigated. It gives a condensation product with phthalic anhydride in the molar ratio 1 : 1. In the presence of picric acid, dihydrazone (II) decomposes and hydrazine picrate is formed.

Our investigation shows that steric hindrance is not present in the formation of cyclohexanedione-1,2 dihydrazone (I) or hexanedione-2,3 dihydrazone (II). This fact was predicted on the basis of a study of models of these compounds. The difficulty of preparing crystalline cyclohexanedione-1,2 dihydrazone (I) apparently is due to the physicochemical properties of the reagent system in which it is observed.

EXPERIMENTAL

Cyclohexanedione-1,2 Dihydrazone (I). Cyclohexanedione-1,2 was prepared by oxidizing cyclohexanone with selenium dioxide [5]. Eight g of anhydrous hydrazine [6] and 20 ml of anhydrous alcohol were put into a three-neck flask provided with a stirrer and dropping funnel and protected from the entrance of moisture. The mixture was cooled to 0° in an ice bath, and a solution of 4 g of cyclohexanedione-1,2 in 20 ml of anhydrous alcohol was added dropwise. The reaction mixture was stirred and cooled for 8 hours, after which it was left for 2 day

at room temperature. The alcohol and excess hydrazine were distilled off in vacuo at a temperature not over 40°. After removal of solvent the residue was placed in an ice bath and very vigorously stirred. After adding a primer (glass powder), light-yellow crystals precipitated, which were dried first by suction and then in a desiccator over $CaCl_2$. M.p. 60-62°. Yield 45%.

Found %: C 51.33, 51.40; H 8.59, 8.64; N 40.04.* M 143. $C_6H_{12}N_4$. Calculated %: C 51.45; H 8.57; N 40.00 M 140.

Cyclohexanedione-1,2 dihydrazone was unstable, turned yellow in the light, and resinified within a few days.

Cyclohexanedione-1,2 Ketazine Dihydrazone (III). A 4.1 g quantity of cyclohexanedione-1,2 and 18 ml of anhydrous alcohol were put into a three-neck flask provided with a dropping funnel and mechanical stirrer. Four g of hydrazine hydrate was added dropwise to the cooled (10-12°) solution. After addition of about two-thirds of the hydrazine hydrate taken, a light-yellow precipitate formed, which dissolved on further addition of hydrazine hydrate. This precipitate could not be studied, since it immediately resinified after removal from the mother liquor. When all the hydrazine hydrate had been added, the reaction mixture was stirred for 6-7 hours at room temperature. The solvent was distilled off in vacuo, and the orange oil obtained was left in the dark in a desiccator over $CaCl_2$ for several months; long, colorless pyramidal crystals with m.p. 178.5° were obtained as a result.

Found %: C 57.95, 58.02; H 8.13, 8.33; N 34.05, 33.65. $C_{12}H_{20}N_6$. Calculated %: C 58.2; H 8.1; N 33.8.

In one case, after standing for 6 months in a desiccator, two large crystals of cyclohexanedione-1,2 dihydrazone, m.p. 60-64° (according to the data of [1], m.p. 63-64°), had formed. The crystals were separated from the mother liquor and put into CCl_4, in which they were kept for several weeks. During this time they changed to the ketazine dihydrazone, m.p. 178.5°, which did not show a melting-point depression with known cyclohexanedione-1,2 ketazine dihydrazone.

Hexanedione-2,3 (acetylbutyryl) was prepared by a modified procedure [4]. Twenty g of hexanone-2 and 2 g of platinum wire catalyst were put into a three-neck flask provided with a reflux condenser and dropping funnel. The contents of the flask were slightly heated, and 42 g of nitric acid (d 1.36) was added. The heating and the rate of addition of acid had to be very carefully regulated, especially in the initial period of the reaction. Excessive heating led to further oxidation of the diketone formed and to decrease in yield; in the extreme case the reaction might proceed explosively.

When all the acid had been added, heating was continued for 30-40 minutes. When the reaction mixture had cooled, the upper, oil layer was separated, washed with a little water, and neutralized with solid potash. After cooling, the diketone was extracted with ether and dried over anhydrous potash. The ether was driven off and the hexanedione-2,3 distilled. Yield 7%. B.p. 42.5-44° (40 mm), $n_D^{18.8}$ 1.4057, d_4^{20} 0.9259.

Hexanedione-2,3 was characterized by preparing the dioxime, m.p. 169-169.5° (according to the data of [4] m.p. 170-171°).

Hexanedione-2,3 Dihydrazone (II). To 8 g of anhydrous hydrazine in 20 ml of anhydrous alcohol, 2.4 g of hexanedione-2,3 in 15 ml of anhydrous alcohol was added dropwise with stirring and cooling. The reaction mixture was left for 2 days for crystallization. The product, after recrystallization from anhydrous methanol and then benzene, had m.p. 59.5-60.3° and consisted of colorless, lamellar crystals. Yield 50%.

Found %: C 50.46, 50.30; H 9.92, 9.97; N 39.55, 39.37; M 133, 147. $C_6H_{14}N_4$. Calculated %: C 50.70; H 9.87; N 39.44. M 142.

The Condensation of Hexanedione-2,3 Dihydrazone (II) With Phthalic Anhydride [8] was carried out in acetic acid. The product was recrystallized from alcohol. M.p. 270-275° (decomp.).

Found %: N 20.4, 20.6. $C_{14}H_{16}O_2N_4$. Calculated %: N 20.58.

Action of Picric Acid on Hexanedione-2,3 Dihydrazone (II). A saturated solution of picric acid in 95% alcohol was added to an aqueous solution of 1 g of the hexanedione dihydrazone (II). The picrate melted at 184.5° and did not show a melting-point depression with known hydrazine picrate.

Found %: N 27.0, 27.2. $C_6H_7O_7N_5$. Calculated %: N 26.9.

* Analyses for nitrogen by the micro-Dumas method were performed in the presence of Berthollet's salt [7].

A Spectrophotometric Investigation of Cyclohexanedione-1,2 Dihydrazone (I) and Hexanedione-2,3 Dihydrazone (II) was carried out in the infrared region with an IKS-11 instrument. The 3 μ region was taken with a LiF prism and the 6 μ region with a NaCl prism. Both dihydrazones were spectrographed in the form of an emulsion of crystals in vaseline. The following maxima, indicating the presence of the NH_2 group in the compounds, were observed.

Cyclohexanedione-1,2 Dihydrazone (I) 3340, 3175, 2960 cm^{-1}; hexanedione-2,3 dihydrazone (II) 3355, 3191, 2976 cm^{-1}.

The spectrum in the 6 μ region could not be interpreted; we could only ascertain that no keto group was present.

SUMMARY

1. Cyclohexanedione-1,2 and hexanedione-2,3 dihydrazones, as well as cyclohexanedione-1,2 ketazine dihydrazone, were prepared and characterized.

2. The interaction of cyclohexanedione-1,2 with hydrazine was investigated. It was shown that, depending on the reaction conditions, either cyclohexanedione-1,2 ketazine dihydrazone or cyclohexanedione-1,2 dihydrazone is formed.

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*Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF SYNTHESIS AND CONVERSIONS IN THE DIARYLCARBAMIDE SERIES

XII. SYNTHESIS OF ANILINES AND DIARYLCARBAMIDES, SIMULTANEOUSLY SUBSTITUTED IN THE NUCLEUS BY CHLORINE AND OTHER SUBSTITUENTS

D. F. Kutepov, D. N. Khokhlov, and V. L. Tuzhilkina

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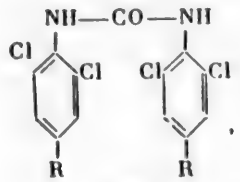
Syntheses of various substituted diarylcarbamides from the corresponding substituted anilines were described earlier [1, 2]. In the phosgenation of 2,6-dichloro-4-nitroaniline it was shown that anilines containing a halogen and a nitro group simultaneously in the nucleus react with difficulty with phosgene, and the corresponding 2,2',6,6'-tetrachloro-4,4'-dinitrodiphenylcarbamide (I) is obtained under quite severe conditions in a yield not over 11% [2]. We continued these investigations, studying the reaction of phosgene with anilines which also contain chlorine atoms in positions 2 and 6 simultaneously but have other substituents in position 4, instead of the nitro group. In this case it was found that the carboxyl or sulfo group in position 4 hinders the reaction of anilines with phosgene even more strongly than the nitro group. Thus, for instance, the corresponding diarylcarbamides cannot be obtained by phosgenation of 2,6-dichloroaminobenzoic or 2,6-dichlorosulfanilic acid under any conditions. Obviously these diarylcarbamides can be prepared by phosgenating 2,6-dichloroaniline and then introducing the corresponding groups in position 4. Compound (I), for instance, has now been obtained by us in about 80% yield by nitrating 2,2',6,6'-tetrachlorodiphenylcarbamide (II), which is not described in the literature and was synthesized by us in 90% yield by phosgenating 2,6-dichloroaniline. In addition, we prepared a number of new diarylcarbamides, analogs of compound (II), with the general formula (A):

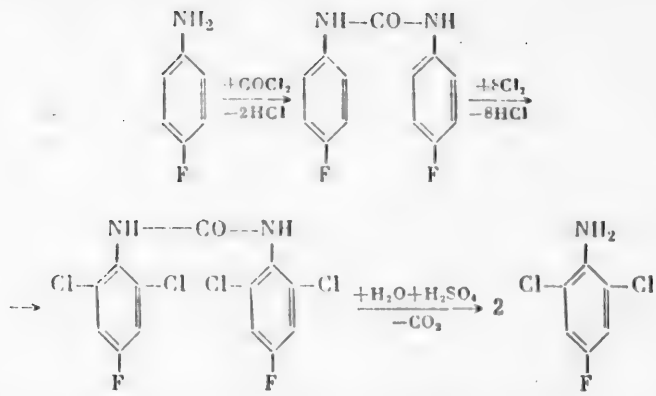


(A)

where R = H (II), F (III), Br (IV), I (V), or CH_3 (VI), and also an isomer of compound (III) – 2,2'-difluoro-4,4', 6,6'-tetrachlorodiphenylcarbamide (VII).

All these diarylcarbamides are prepared relatively easily by phosgenating the corresponding anilines in an inert solvent, with heating. Certain of the anilines are not described in the literature and were prepared by us for the first time.

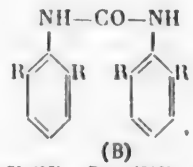
The 4-fluoro-2,6-dichloroaniline required for the synthesis of compound (III) was prepared according to the scheme



Proceeding from o-fluoroaniline, the 2-fluoro-4,6-dichloroaniline required for the synthesis of compound (VII) was similarly prepared. According to literature data [3], 2,6'-dichloro-4-bromoaniline is formed by chlorinating p-bromoaniline with N-chloro-2,4-dichloroacetanilide. We could not obtain it in satisfactory yield by this method, since substitution of bromine by chlorine takes place on chlorination. This aniline is much more easily obtained in good yield by brominating 2,6-dichloroaniline in acetic acid.

We prepared the 2,6-dichloro-4-iodoaniline required for the synthesis of compound (V) by iodinating 2,6-dichloroaniline with iodine monochloride in acetic acid.

We also prepared diarylcarbamides with the general formula (B) by phosgenating the corresponding anilines:



(B)

where: R = Cl (II), Br (VIII), CH_3 (IX).

Most of the substituted anilines and substituted diarylcarbamides synthesized by us have not been described before in the literature.

EXPERIMENTAL

2,2',6,6'-Tetrachloro-4,4'-dinitrodiphenylcarbamide (I). Seven g of (II) was dissolved at room temperature in 45 ml of concentrated sulfuric acid. A mixture of 3 ml of fuming nitric acid (d 1.5) and 10 ml of concentrated sulfuric acid was added to the solution, with stirring, and the reaction mixture was kept at room temperature for 30 minutes and then poured into ice water. The precipitated product was filtered out, and washed with water and acetone. There was obtained 7 g of a white powder (79.5%), m.p. 252-253° (decomp.). According to the data of [2] m.p. 250-251° and yield 11%.

Found %: N 12.13, 12.17; Cl 32.51, 32.44. $C_{13}H_6O_5N_4Cl_4$. Calculated %: N 12.74; Cl 32.23.

2,2',6,6'-Tetrachlorodiphenylcarbamide (II). Twenty g of 2,6-dichloroaniline was dissolved in 200 ml of chlorobenzene or trichlorobenzene, and phosgene was passed into the solution at 100° for 2 hours, with stirring. On the next day the precipitate formed was filtered out, and washed with benzene and alcohol. There was obtained 19.4 g (90%) of a white powder with m.p. 293-295° (in a sealed capillary). After recrystallization from glacial acetic acid the melting point was unchanged.

Found %: C 44.54, 44.72; H 2.09, 2.11; N 7.84, 7.95; Cl 39.19, 39.23. $C_{13}H_8ON_2Cl_4$. Calculated %: C 44.61; H 2.30; N 8.00; Cl 40.52.

4,4'-Difluoro-2,2',6,6'-tetrachlorophenylcarbamide (III). Preparation of 4,4'-difluorodiphenylcarbamide. Twenty g of 4-fluoroaniline in 100 ml of dichloroethane, 70 ml of water, and 20 g of sodium carbonate were put

into the reaction vessel, and phosgene was passed in for 2 hours, with stirring and cooling. The temperature in the reaction vessel was kept between 20 and 30°. On the next day the precipitate was filtered out, and washed with water. After drying there was obtained 18 g (86.1%) of a white powder, which was recrystallized from glacial acetic acid. M.p. 260-263° (in a sealed capillary).

Found %: C 63.30, 63.38; H 4.05, 4.17; N 11.14, 11.10; F 13.90, 14.15. $C_{13}H_{10}ON_2F_2$. Calculated %: C 62.90; H 4.02; N 11.28; F 15.31.

b) Preparation of 4-fluoro-2,6-dichloroaniline. Into a reaction vessel containing 20 g of 4,4'-difluorodiphenylcarbamide and 240 ml of glacial acetic acid, chlorine was passed for 6 hours at 80°, with stirring. At the beginning of the chlorination all the diphenylcarbamide dissolved, but later a bulky precipitate formed. Toward the end of the chlorination the contents of the reaction vessel were cooled, and the precipitate was filtered out, washed with acetic acid and water, and dried. There was obtained 20.3 g of a white powder consisting of substance (III) with an admixture of a less-chlorinated product. For hydrolysis and deanilination 20 g of crude substance (III) was heated in 100 ml of concentrated sulfuric acid at 165-170° for 40 minutes, cooled, and poured into 1 ml of cold water, and the precipitated 4-fluoro-2,6-dichloroaniline was filtered out or removed by steam distillation. There was obtained 13.3 g of a substance with m.p. 59-60° (from 50% alcohol).

Found %: C 40.35, 40.50; H 2.20, 2.60; N 7.65, 7.92; F 9.91, 9.77. $C_6H_4NFCl_2$. Calculated %: C 40.03; H 2.23; N 7.78; F 10.56.

c) Preparation of (III). A slow current of phosgene was passed for 3 hours through a solution of 5 g of 4-fluoro-2,6-dichloroaniline in 30 ml of chlorobenzene, heated to 105-110°. The precipitate formed was filtered out, and washed with benzene and acetone. There was obtained 3.2 g (59.9%) of a white powder, m.p. 290-291° (in a sealed capillary).

Found %: C 41.05, 41.18; N 6.83, 6.60; Cl 36.62, 36.81. $C_{13}H_6ON_2F_2Cl_4$. Calculated %: C 40.44; N 7.26; Cl 36.74.

2,2',6,6'-Tetrachloro-4,4'-dibromodiphenylcarbamide (IV). a) Preparation of 2,6-dichloro-4-bromoaniline. Six g of 2,6-dichloroaniline was dissolved in 60 ml of glacial acetic acid, and 6 g of bromine in 20 ml of acetic acid was added slowly, with stirring, at a temperature not over 10°. The precipitate formed was filtered out, washed with water, and dried at room temperature. There was obtained 6.6 g (73.8%) of dichlorobromoaniline, m.p. 86-87°. According to data of [3] m.p. 85°.

b) Preparation of (IV). A slow current of phosgene was passed for 1.5 hours through a solution of 2 g of 2,6-dichloro-4-bromoaniline in 10 ml of trichlorobenzene, heated to 110-120°. After this the solution was kept at the same temperature for 2.5 hours more and then left overnight at room temperature. The precipitate formed was filtered out, and washed with benzene and alcohol. There was obtained 0.7 g (33.1%) of (IV). It sublimed at 298-299°. M.p. 285° (in a sealed capillary).

Found %: C 31.72, 31.80; H 1.09, 1.18; N 5.04, 5.23. $C_{13}H_6ON_2Cl_4Br_2$. Calculated %: C 30.72; H 1.18; N 5.50.

2,2',6,6'-Tetrachloro-4,4'-diiododiphenylcarbamide (V). a) Preparation of 2,6-dichloro-4-iodoaniline. Ten g of 2,6-dichloroaniline was dissolved in 120 ml of glacial acetic acid. Then 1.5 ml of water, and 10 g of iodine monochloride in 30 ml of glacial acetic acid were added to the solution, and the latter was boiled for 10 minutes. On the next day sodium bisulfite solution was added, with stirring, until the iodine color disappeared. The precipitate was filtered out, washed with water, and recrystallized from 30% alcohol. There was obtained 11.7 g of 2,6-dichloro-4-iodoaniline of a light-lilac color, m.p. 96-97°. On further recrystallization the melting point did not change.

Found %: C 25.52, 25.18; H 1.54, 1.69; N 4.76, 5.09; Cl + I (converted to Cl), 35.12, 35.09. $C_6H_4NCl_2I$. Calculated %: C 25.03; H 1.40; N 4.86; Cl + I (converted to Cl) 36.77.

b) Preparation of (V). Five g of 2,6-dichloro-4-iodoaniline was dissolved in 50 ml of xylene, the solution heated to 100°, and phosgene passed in for 20 minutes. The solution was cooled to room temperature, saturated with phosgene, and left for several weeks. Within 3-5 days a precipitate formed, the amount of which gradually increased. Without waiting for the end of the reaction the precipitate was filtered out and washed with benzene, the mother liquor being saved in order to obtain an additional quantity of (V). The yield was good. The substance was a white powder, insoluble in common solvents, and it could not be recrystallized. On heating to 300° it did not melt.

Found %: C 26.18, 26.48; H 1.55, 1.26; N 4.55, 4.71; Cl + I (converted to Cl) 36.14, 36.31. $C_{13}H_6ON_2Cl_4I_2$. Calculated %: C 25.94; H 1.01; N 4.65; Cl + I (converted to Cl) 35.35.

2,2',6,6'-Tetrachloro-4,4'-dimethyldiphenylcarbamide (VI). This was prepared similarly to (IVb). From 1 g of 2,6-dichloro-4-methylaniline, 0.2 g (18.8%) of a white powder was obtained. When the reaction was carried out in a medium consisting of the mother liquor from the preceding reaction, the yield rose to 66.0%. Substance (VI) was insoluble in common solvents and could not be recrystallized. At 284° it sublimed.

Found %: C 47.40, 46.97; H 3.40, 3.02; N 6.80, 6.75; Cl 36.30, 36.45. $C_{15}H_{12}ON_2Cl_4$. Calculated %: C 47.61; H 3.17; N 7.40; Cl 37.56.

2,2'-Difluoro-4,4',6,6'-tetrachlorodiphenylcarbamide (VII). a) 2,2'-Difluorodiphenylcarbamide was prepared similarly to (IIIa). Ten g of 2-fluoroaniline gave 9.2 g (88%) of a white powder. M.p. 240-242° (in a sealed capillary).

Found %: C 63.70, 63.79; H 4.10, 4.33; N 11.22, 11.06; F 14.07, 14.30. $C_{13}H_{10}ON_2F_2$. Calculated %: C 62.90; H 4.02; N 11.28; F 15.31.

b) 2-Fluoro-4,6-dichloroaniline was prepared similarly to (IIIb). Seven g of 2,2'-difluorodiphenylcarbamide gave 3.6 g of fluorodichloroaniline, which after recrystallization from 50% alcohol melted at 60-61°.

Found %: C 40.44, 40.82; N 7.55, 7.66; F 9.17. $C_6H_4NFCl_2$. Calculated %: C 40.03; N 7.78; F 10.56.

c) Compound (VII) was prepared similarly to (IIIc). Three g of 2-fluoro-4,6-dichloroaniline gave 0.8 g (23.5%) of a white powder, m.p. 298-300° (in a sealed capillary).

Found %: N 7.17, 7.31; F 9.42; Cl 36.12, 36.32. $C_{13}H_6ON_2F_2Cl_4$. Calculated %: N 7.26; F 9.84; Cl 36.74.

2,2',6,6'-Tetrabromodiphenylcarbamide (VIII). This was prepared similarly to (IVb) at 90-100°. Five g of 2,6-dibromoaniline gave 2.5 g (47.5%) of a white powder. When the reaction was repeated, the mother liquor from the reaction carried out earlier being used as solvent, the yield increased to 93%. The product did not melt. It sublimed at 299-300°.

Found %: C 30.10, 30.34; H 1.85, 2.03; N 5.07, 5.16; Br 60.70, 69.18. $C_{13}H_8ON_2Br_4$. Calculated %: C 29.56; H 1.51; N 5.31; Br 60.57.

2,2',6,6'-Tetramethyldiphenylcarbamide (IX). A 0.5 g quantity of 2,6-dimethylaniline was phosgenated with vigorous stirring in 20 ml of water for 30 minutes, soda solution being added gradually to neutralize the hydrogen chloride formed in the reaction. There was obtained 0.47 g (85%) of a white powder. M.p. 321-323° (decom

Found %: C 75.88, 75.85; H 8.24, 7.99; N 10.49, 10.55. $C_{17}H_{20}ON_2$. Calculated %: C 76.08; H 7.51; N 10.44.

SUMMARY

1. A number of new substituted anilines and diarylcarbamides, containing chlorine and other substituents simultaneously in the nucleus, were synthesized.

2. It was shown that such substituents as the nitro, carboxyl, and sulfo groups, situated in the nucleus of the aniline, strongly hinder its reaction with phosgene.

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INVESTIGATION IN THE FIELD OF SYNTHESIS AND CONVERSIONS IN THE DIARYLCARBAMIDE SERIES

XIII. INTERACTION OF HEXACHLORODIPHENYLCARBAMIDES WITH ANILINE

D. F. Kutepov and A. A. Potashnik

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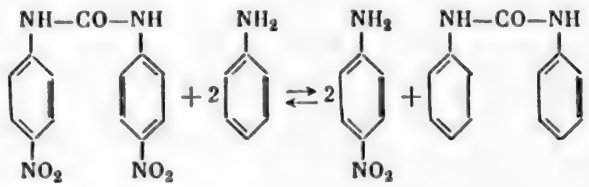
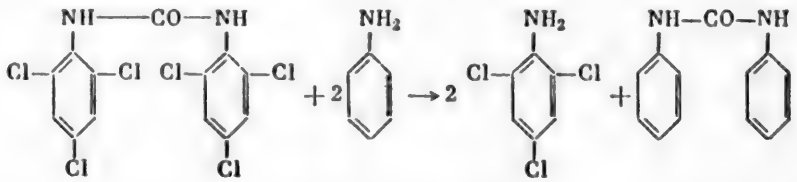
Exchange reactions between diphenylcarbamide and its derivatives and a number of primary aromatic amines [1], and reactions of transamidation of carboxylic acid amides [2], are described in the literature. The reaction of 4,4'-dinitrodiphenylcarbamide with aniline was investigated in detail earlier [3]. In this case it was found that under optimum conditions the reaction goes with a nearly quantitative yield of p-nitroaniline and diphenylcarbamide. Moreover, this reaction was shown to be reversible.



However, the reverse reaction goes with much greater difficulty than the forward, and a large excess of p-nitroaniline is required in order to carry it out. From literature data [4] it is also known that aromatic monosubstituted arylcarbamides are converted to symmetrical diarylcarbamides by heating to their melting points. The rates and degrees of conversion depend on the conditions under which the process takes place.

In the present work we investigated the interaction of hexachlorodiphenylcarbamides with aniline. This reaction is not described in the literature and is of interest.

When a mixture of 2,2',4,4',6,6'-hexachlorodiphenylcarbamide and aniline is heated, the reaction goes according to the equation

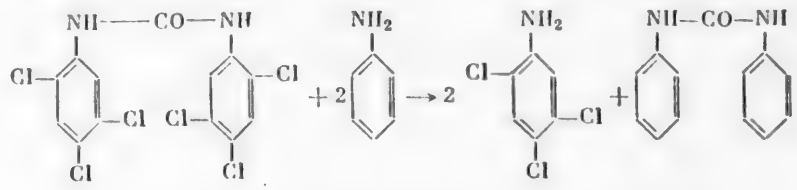


Yields of 2,4,6-trichloroaniline and diphenylcarbamide reach 97%. The optimum quantity of aniline is 185% of theoretical; when the quantity of aniline is increased to 300%, the yield of trichloroaniline sharply falls. The

Expt. No.	Amount taken of			Reaction time (in min)	Yield of 2,4,6-trichloroaniline (in %)	Melting point	Yield of diphenylcarbamide (in %)	Melting point
	hexachlorodiphenylcarbamide (in g)	aniline (in g)	aniline (in % of theoretical)					
1	4	15	Large excess	30	80.8	78°	91.5	235°
2	4	3.55	200	30	49.5	78	65.6	239
3	10	13.3	300	30	76.3	76	72.5	236
4	10	9	200	60	62.0	78	73.8	235
5	6.5	5.2	185	180	92.1	78	97.0	237
6	6.5	5.2	185	180	97.37	78	90.57	239

optimum temperature is 180-190°; lowering the temperature to 150° slows the reaction, whereas raising it to 200° leads to greater resinification of the reaction mass and a diminished yield of final products. The reaction time is 3 hours or less. When the reaction time is decreased to 30 minutes, the process does not go to completion.

We also investigated the reaction of 2,2',4,4',5,5'-hexachlorodiphenylcarbamide with aniline, which goes according to the equation



In this case 2,4,5-trichloroaniline and diphenylcarbamide are formed in 92% yield.

The mechanism of the interaction of hexachlorodiphenylcarbamides with aniline may be represented by the scheme

$$(I)\quad C_6H_2Cl_3NHCONHC_6H_2Cl_3 \rightleftarrows C_6H_2Cl_3NH_2 + C_6H_2Cl_3NCO$$
$$(II)\quad C_6H_2Cl_3NCO + C_6H_5NH_2 \longrightarrow C_6H_2Cl_3NHCONHC_6H_5$$
$$(III)\quad C_6H_2Cl_3NHCONHC_6H_5 \longrightarrow C_6H_2Cl_3NH_2 + C_6H_5NCO$$
$$(IV)\quad C_6H_5NCO + C_6H_5NH_2 \longrightarrow C_6H_5NHCONHC_6H_5$$

The formation of trichlorophenyl isocyanate on heating of hexachlorodiphenylcarbamide was proved by us experimentally. For this purpose hexachlorodiphenylcarbamide was heated in decalin; the 2,4,6-trichlorophenyl isocyanate formed under these conditions was combined with 2,4-dichloroaniline, and the resulting compound — 2,2',4,4',6-pentachlorodiphenylcarbamide — was isolated in pure form.

EXPERIMENTAL

1. Reaction of 2,2',4,4',6,6'-Hexachlorodiphenylcarbamide with Aniline. A mixture of hexachlorodiphenylcarbamide and aniline was heated at 180-190°. The reaction mass was cooled to 25° and the excess aniline removed with hydrochloric acid, and the precipitate was then washed with water and alcohol. Diphenylcarbamide was left on the filter; dilution of the alcoholic filtrate with water resulted in the formation of a 2,4,5-trichloroaniline precipitate, which was recrystallized. Results of the experiments are given in the table.

In Experiments 5 and 6 aniline and 2,4,6-trichloroaniline were steam distilled from the reaction mass.

2. Reaction of 2,2',4,4',5,5'-Hexachlorodiphenylcarbamide with Aniline. A mixture of 6.38 g of hexachlorodiphenylcarbamide and 5 g (185%) of aniline was heated at 180° for 3 hours. Then the excess aniline and 1.18 g of 2,4,5-trichloroaniline, m.p. 96°, were removed by steam distillation. After filtration of the reaction

mass a 7.4 g residue (mixture of trichloroaniline and diphenylcarbamide) was obtained. This residue gave 5.93 g of material, which was washed several times with alcohol. As a result there was obtained 2.51 g (98%) of diphenylcarbamide, m.p. 237°; after recrystallization from glacial acetic acid, m.p. 239°.

Found %: C 72.48, 73.24; H 6.08, 5.95; N 13.47, 12.98. $C_{13}H_{12}ON_2$. Calculated %: C 73.58; H 5.66; N 13.2.

The alcoholic washings were evaporated to dryness. This resulted in a 3.6 g residue with m.p. 96.5° after recrystallization, which corresponds to the melting point of 2,4,5-trichloroaniline. A mixed sample of the substance obtained with 2,4,5-trichloroaniline showed no melting-point depression.

3. Thermal Decomposition of 2,2',4,4',6,6'-Hexachlorodiphenylcarbamide. Fifteen g of hexachlorodiphenylcarbamide in 300 ml of decalin was heated at 195-200° for 10 hours. A 1.55 g quantity of undecomposed hexachlorodiphenylcarbamide was filtered out of the reaction mass. The products formed, dissolved in 300 ml of decalin, were heated to 120°, i.e., the decomposition temperature of the hexachlorodiphenylcarbamide [5], and at this temperature 6.8 g of phosgene was passed into the solution during 45 minutes in order to react with the 2,4,6-trichloroaniline formed. As a result there was obtained 6.2 g of a substance with m.p. 290°, or 320° after recrystallization (hexachlorodiphenylcarbamide). The 2,4,6-trichlorophenyl isocyanate remaining in the solution was isolated by condensation with 2,4-dichloroaniline, in the form of 2,4,6,2',4'-pentachlorodiphenylcarbamide. For this purpose part of the solution (80 ml) was blown out with air to remove excess phosgene, and then treated at 50° with 1.5 g of 2,4-dichloroaniline dissolved in 15 ml of dry dichloroethane. The mixture was kept at this temperature for 3.5 hours. The precipitate formed was filtered out, washed with dichloroethane, and dried at 60°. There was obtained 2.2 g of a substance with m.p. 250°, which corresponds to 2,4,6,2',4'-pentachlorodiphenylcarbamide [6]. A mixed sample with pentachlorodiphenylcarbamide showed no depression.

Found %: Cl 46.15; 46.00. $C_{13}H_7ON_2Cl_5$. Calculated %: Cl 45.11.

SUMMARY

1. The reaction of hexachlorodiphenylcarbamide with anilines was studied; in this case it was shown that this reaction gives very high yields of trichloroanilines and diphenylcarbamide.

2. A mechanism has been proposed for the reaction of hexachlorodiphenylcarbamide with anilines.

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CATALYTIC CONDENSATION OF SCHIFF BASES WITH METHYL p-TOLYL KETONE. VI.

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Previously, in a number of our communications [1, 2] we presented experiments on the catalytic condensation of Schiff bases with ketones. The present study is a continuation of previous investigations, here on the reaction of condensation of various Schiff bases with methyl p-tolyl ketone.

This investigation shows that the nature of the final reaction product is determined by the chemical nature of the Schiff base and the conditions of carrying out the reaction. Thus, in the condensation of methyl p-tolyl ketone with the Schiff base obtained from aromatic aldehydes and aniline, its homologs and derivatives, the sole reaction product under our conditions is the corresponding β-arylamino-ketone. For example, in the condensation of benzalaniline with methyl p-tolyl ketone we obtained p-tolyl-[β-(anilino)-β-phenylethyl]-ketone. It is pertinent to remark that this product was obtained earlier in an analogous way but in the presence of an alkaline catalyst, but Mayer [3] reports a melting point of 173° for this substance, and Weygand [4] gives 141°. Our work shows that this compound melts at 142°.

From benzal-p-toluidine and methyl p-tolyl ketone we synthesized p-tolyl-[β-(p-toluidino)-β-phenylethyl]-ketone (II). In the reaction of benzal-m-toluidine we prepared p-tolyl-[β-(m-toluidino)-β-phenylethyl]-ketone (III). In the condensation of benzal-p-anisidine with methyl p-tolyl ketone we obtained p-tolyl-[β-(p-anisidino)-β-phenylethyl]-ketone (IV). From benzal-p-phenetidine and the p-tolyl ketone we synthesized p-tolyl-[β-(p-phenetidino)-β-phenylethyl]-ketone (V). In the condensation of benzal-m-nitroaniline with methyl p-tolyl ketone we synthesized p-tolyl-[β-(m-nitroanilino)-β-phenylethyl]-ketone (VI), and finally, from benzal-p-nitroaniline and methyl p-tolyl ketone we prepared p-tolyl-[β-(p-nitroanilino)-β-phenylethyl]-ketone (VII). The last six compounds were first synthesized by us.

The synthesis of all the above-mentioned compounds can be considered as the result of addition of a molecule of ketone containing a mobile hydrogen atom to the azomethine bond of the Schiff base, which can be represented as follows.

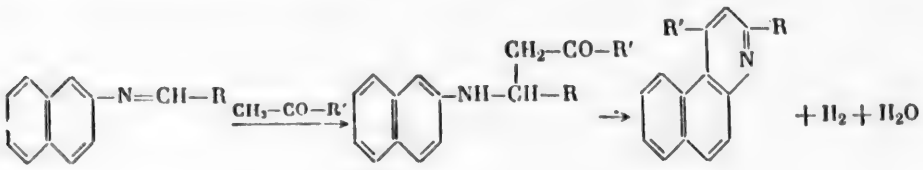
$$R-C_6H_4N{=}CH-C_6H_5 \xrightarrow{CH_2-CO-R'} R-C_6H_4NH-\underset{\displaystyle CH_2-CO-R'}{\underset{|}{CH}}-C_6H_5$$

When our synthesized β-arylaminoketones are heated with concentrated hydrochloric acid, they undergo hydramine splitting according to the following scheme

$$R-C_6H_4NH-\underset{\displaystyle CH_2-CO-R'}{\underset{|}{CH}}-C_6H_5 \xrightarrow{H^+} R-C_6H_4NH_2 + C_6H_5CH{=}CH-CO-R'$$

As we already mentioned before, [1, 2], the Schiff bases obtained from 2-naphthylamine and aromatic aldehydes react very specifically with aliphatic aromatic ketones. Depending on the chemical nature of the Schiff base and the reaction conditions, we can obtain the corresponding β-arylaminoketone or a derivative of 2-phenyl-5,6-benzoquinoline. This is explained by the fact that arylaminoketones which contain a 2-naphthylamine residue in the β-position do not undergo hydraminic splitting, but have the exclusive ability to cyclize into the corresponding derivative of 5,6-benzoquinoline [5]. Thus, under relatively mild reaction conditions (heating 15-20 minutes) benzal-2-naphthylamine and methyl p-tolyl ketone from p-tolyl-[β-(2-naphthylamino)-β-phenylethyl] ketone (VIII). However if the reaction is run for a longer time and in a sealed tube, the chief reaction product is 2-phenyl-4-(4-methylphenyl)-5,6-benzoquinoline (IX). The latter substance is the product of cyclization of p-tolyl-β-(2-naphthylamino)-β-phenylethylketone. We confirmed this idea by special experiments. By the same process we succeeded in condensing benzal-2-naphthylamine with methyl p-tolyl ketone under new conditions to obtain 2-phenyl-4-(4-methylphenyl)-5,6-benzoquinoline (IX); in the condensation of m-nitrobenzal-2-naphthylamine with methyl p-tolyl ketone we synthesized 2-m-nitrophenyl-4-(4-methylphenyl)-5,6-benzoquinoline (X), in the condensation of p-nitrobenzal-2-naphthylamine with methyl p-tolyl ketone we succeeded in obtaining 2-p-nitrophenyl-4-(4-methylphenyl)-5,6-benzoquinoline (XI), and in the reaction of p-dimethylaminobenzal-2-naphthylamine with methyl p-tolyl ketone we synthesized 2-p-dimethylaminophenyl-4-(4-methylphenyl)-5,6-benzoquinoline (XII). All the substances mentioned by us in this series were obtained for the first time here.

The mechanism of this reaction can be represented as follows



All these reactions have a catalytic character; the catalysts in these reactions are the salts of those primary aromatic amines which enter the composition of the Schiff base used in the chemical reaction.

EXPERIMENTAL

The starting substances, the Schiff bases, were obtained by the usual method, except for benzal-m-nitroaniline and benzal-p-nitroaniline which were synthesized by the method of [6]. Methyl p-tolyl ketone was prepared according to the literature [7].

1. Synthesis of β-arylaminoketones was carried out in two variants: in the first variant the reaction mass of 0.01 mole Schiff base, 0.01 mole of methyl p-tolyl ketone, 10 ml of alcohol, and 1.0 g of the hydrochloride of the amine in the Schiff base was heated on a water bath for 30-40 minutes in a flask with a reflux condenser. After cooling, the crystals which separated were filtered off, treated to an alkaline reaction with a weak solution of ammonia, and crystallized from a mixture of alcohol and benzene.

In the second variant the reaction mass was heated 30-40 minutes on a water bath in a sealed tube. All the rest of the treatment of the reaction product was as described above. We consider the second variant more suitable since it gives somewhat higher yields of reaction product and the latter is obtained in purer form. Therefore the synthesis of the β-arylaminoketones which we synthesized are given in the table.

Hydramine splitting of the β-arylaminoketones was carried out as follows: 0.1-0.3 g of β-arylaminoketone and 5.0 ml of concentrated hydrochloric acid were heated with shaking on a boiling water bath to complete disappearance of the solid β-arylaminoketone into a melted surface oil. As a rule, this took not more than 2-10 minutes. After cooling in a refrigerator the oil crystallized. Then the acid was poured off, the crystals were washed with cold water and recrystallized from alcohol. The resulting substance had m.p. 55°. A mixed sample of this substance with commerical known 4'-methylchalcone [8] showed no melting point depression.

2. Synthesis of β-(2-naphthylamino)-β-phenylethyl ketone (VIII). The reaction mass from 5 g of benzal-2-naphthylamine, 3 g of methyl p-tolyl ketone, 10 ml of alcohol, and 1.0 g of 2-naphthylamine hydrochloride

Name and formula of synthesized β-arylaminoketones	M.p.	Yield, %	% N	
			calculated	found
p-Tolyl-[β-(anilino)-β-phenylethyl]-ketone $C_{22}H_{31}ON$ (I)	142°	28.6	4.44	4.30, 4.23
p-Tolyl-[β-(p-toluidino)-β-phenylethyl]-ketone $C_{23}H_{23}ON$ (II)	151	54.3	4.25	4.18, 4.09
p-Tolyl-[β-(m-toluidinol)-β-phenylethyl]-ketone $C_{23}H_{23}ON$ (III)	114	48.5	4.25	4.02, 4.02
p-Tolyl-[β-(p-anisidino)-β-phenylethyl]-ketone $C_{23}H_{23}O_2N$ (IV)	120	43.4	4.06	4.15, 4.06
p-Tolyl-[β-(p-phenetidino)-β-phenylethyl]-ketone $C_{24}H_{25}O_2N$ (V)	129 – 130	60.0	3.90	4.18, 4.13
p-Tolyl-[β-(m-nitroanilino)-β-phenylethyl]-ketone $C_{22}H_{20}O_3N_2$ (VI)	130	52.8	7.77	7.64, 7.84
p-Tolyl-[β-(p-nitroanilino)-β-phenylethyl]-ketone $C_{22}H_{20}O_3N_2$ (VII)	158	45.7	7.77	7.62, 7.81

was heated in a beaker for 10 minutes on a water bath. After treatment we obtained 2.7 g (34.3%) of a substance with m.p. 186° from benzene.

Found %: N 3.82, 3.96. $C_{26}H_{23}ON$. Calculated %: N 3.84.

3. Synthesis of 2-phenyl-4-(4-methylphenyl)-5,6-benzoquinoline (IX). Two g of β-(2-naphthylamino)-β-phenylethyl ketone was heated 30 minutes on the water bath with 5.0 ml of concentrated hydrochloric acid. After cooling, the reaction mass was neutralized with a solution of alkali, the isolated product was crystallized from a mixture of alcohol and benzene. We obtained 1.1 g (60%) of a substance with m.p. 148° from benzene.

Found %: N 4.17, 4.21. $C_{26}H_{19}N$. Calculated %: N 4.06.

Hydrochloride m.p. 212°. Picrate m.p. 254°.

Analysis of chloroplatinate. Found %: Pt 17.61. $(C_{26}H_{19}N)_2 \cdot H_2Cl_6Pt$. Calculated %: Pt 17.70.

The synthesis of 5,6-benzoquinoline derivatives was also carried out in two variants. In the first variant the reaction between the Schiff base from 2-naphthylamine and methyl p-tolyl ketone was carried out in alcohol solution at 100° in a sealed tube. Below we give examples of synthesis by this first variant.

4. Synthesis of 2-phenyl-4-(4-methylphenyl)-5,6-benzoquinoline in one step. The reaction mass from 2.3 g of benzal-2-naphthylamine, 1.4 g of methyl p-tolyl ketone, 5.0 ml of alcohol, and 1.0 g of 2-naphthylamine hydrochloride was heated on a boiling water bath for 30 minutes in a sealed tube. We obtained 1.2 g (14.0%) of substance with m.p. 148°. A sample mixed with the product obtained in the previous experiment gave no melting point depression. Hydrochloride m.p. 212°, picrate m.p. 254°.

5. Synthesis of 2-(3-nitrophenyl)-4-(4-methylphenyl)-5,6-benzoquinoline (X). In the reaction we took 4.0 g of m-nitrobenzal-2-naphthylamine, 2.2 g of methyl p-tolyl ketone, 5.0 ml of alcohol, and 1.0 g of 2-naphthylamine hydrochloride. The reaction was carried out in the same way as in the preceding experiment. We obtained 1.8 g (30%) of a substance with m.p. 238° from benzene.

Found %: N 7.02, 7.17. $C_{26}H_{18}O_2N_2$. Calculated %: N 7.18.

Picrate m.p. 224°.

6. Synthesis of 2-(4-nitrophenyl)-4-(4-methylphenyl)-5,6-benzoquinoline (XI). In the reaction we took 2.3 g of p-nitrobenzal-2-naphthylamine, 1.4 g of methyl p-tolyl ketone, 5 ml of alcohol, and 0.5 g of 2-naphthylamine hydrochloride. We obtained 1.6 g (50%) of a substance with m.p. 195°. The substance was poorly soluble in alcohol, weakly so in benzene.

Found %: N 7.02, 7.24, $C_{26}H_{18}O_2N_2$. Calculated %: N 7.18.

Picrate m.p. 275° (decomposition).

7. Synthesis of 2-(4-dimethylaminophenyl)-4-(4-methylphenyl)-5,6-benzoquinoline (XII). From 2 g of p-dimethylaminobenzal-2-naphthylamine, 1.2 g of methyl p-tolyl ketone in the presence of 0.5 g of 2-napthylamine hydrochloride we obtained 0.9 g (30%) of a substance with m.p. 196° from alcohol. The substance was poorly soluble in alcohol, easily so in benzene with a blue fluorescence.

Found %: N 7.26, 7.02. $C_{28}H_{24}N_2$. Calculated %: N 7.22.

Picrate was orange, m.p. 232° (decomposition); hydrochloride m.p. 235° (decomposition).

In the second variant the synthesis of the 5,6-benzoquinoline derivatives was carried out by heating the Schiff bases from 2-naphthylamine with methyl p-tolyl ketone in the absence of a solvent and by heating the reaction mass on an oil bath for 30 minutes at 170-175°. However, in the second variant, the yield of quinoline bases was somewhat lower, and the reaction products were much less pure; therefore we recommend the use of the first variant in the synthesis of 5,6-benzoquinoline derivatives.

SUMMARY

1. We have studied the reaction of catalytic condensation of methyl p-tolyl ketone with benzalaniline, benzal-m-toluidine, benzal-p-toluidine, benzal-p-anisidine, benzal-p-phenetidine, benzal-m-nitroaniline, benzal-p-nitroaniline, and benzal-2-naphthylamine. We have obtained the corresponding β-arylaminoketones.

2. We have studied the reaction of catalytic condensation of methyl p-tolyl ketone with benzal-2-naphthylamine, m-nitrobenzal-2-naphthylamine, p-nitrobenzal-2-naphthylamine and with p-diemthylaminobenzal-2-napthylamine. We have synthesized the corresponding derivatives of 2-phenyl-5,6-benzoquinoline.

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SYNTHESIS OF VINYL MONOMERS.

XI. SYNTHESIS OF α-CHLOROHYDROACRYLATES AND α-CHLOROACRYLATES

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Derivatives of α-chlorohydracrylic acid are little known and most of the information about them is in the patent literature [1]. α-Chloro-β-hydroxy- propionic acid itself was described earlier [2].

Below we describe the synthesis of the methyl ester of α-chlorohydroacrylic acid and the nitrile of this acid by direct treatment of methyl acrylate and acrylonitrile with hypochlorite. Methyl α-chlorohydracrylate easily dehydrates to give good yields of methyl α-chloroacrylate. This method for its synthesis has some advantages over the usual synthesis from methyl α,β-dichloropropionate. Among other derivatives of α-chloroacrylic acid we have synthesized the phenyl ester by a modified method of Marvel et al., [3]. In describing this ester, the authors give for it n_D^{20} 1.5808. However, this value is incorrect. We have found a value of nD^{20} 1.5325 which fits well into the series of values for the refractive indexes of α-haloacrylates and seems to us more correct.

In the dehydration of our chlorohydroxypropionitrile, α-chloroacrylonitrile is formed. The results of the dehydration show that treatment of acrylates with hypochlorites leads to formation of α-chlorohydracrylates and not the isomeric β-chlorolactates.

EXPERIMENTAL

α-Chloro-β-hydroxypropionitrile. We dissolved 128 g of acrylonitrile in 2 liters of water at 16° and with stirring introduced chlorine into the solution at a rate which easily exceeded the rate of its absorption. When, after 24 hours, the rate of chlorine absorption decreased, 64 g of acrylonitrile was added and the reaction was continued for another 29 hours. The excess of dissolved chlorine was removed from the solution by bubbling air through it, the α-chloro-β-hydroxypropionitrile was extracted with ether (five portions of 200 ml) which was dried over anhydrous sodium sulfate and distilled off. We obtained 133.5 g (38.5%).

B.p. 112° (11 mm), d_4^{20} 1.3028, n_D^{20} 1.4619, MR_D 22.35; Calc. 22.36.

Found %: C 34.45; H 4.14; Cl 33.71; N 12.78. C_3H_4ONCl. Calculated %: C 34.1; H 3.1; Cl 33.6; N 13.3.

α-Chloro-β-acetoxypropionitrile. A mixture of 5 g of α-chloro-β-hydroxypropionitrile, 8.25 g of acetic anhydride, and 0.65 g of fused sodium acetate was heated on a boiling water bath for two hours. After cooling, the reaction mass was poured into 15 ml of cold water. The organic layer was separated, dried with anhydrous sodium sulfate, and vacuum distilled. We obtained 3.9 g (55.8%).

B.p. 77.5-79° (5 mm), d_4^{20} 1.2221, n_D^{20} 1.4391, MR_D 31.5; Calc. 31.1.

Found %: Cl 23.90. C_5H_5ONCl. Calculated %: Cl 24.1.

Methyl α-chloro-β-hydroxypropionate. After 24 hours chlorination of a solution of 66 g of redistilled methylacrylate in 1.5 liters of water under the conditions described in experiment 1 and analogous treatments of the reaction product, we obtained 25 g (23.5%) of substance.

B.p. 106° (20 mm), d_4^{20} 1.3203, n_D^{20} 1.4539, MR_D 28.75; Calc. 28.15.

Found %: C 33.85; H 3.91; Cl 25.3. $C_4H_7O_2Cl$. Calculated %: C 33.7; H 5.0; Cl 25.7.

Methyl α-chloroacrylate. a) To a mixture of 5 g of sulfuric acid and 0.3 g of cuprous chloride heated to 125-130° was gradually added 5 g methyl α-chloro-β-hydroxypropionate, upon which 3.79 g of methyl α-chloroacrylate distilled off and was dried and distilled. We obtained 3.2 g (74%) of pure product.

B.p. 57-60° (55 mm), n_D^{20} 1.4420.

Found %: Cl 29.0. $C_4H_5O_2Cl$. Calculated %: Cl 29.4.

b) To a mixture of 2 g of phosphorus pentoxide and 0.2 g of cuprous chloride was gradually added 5 g of methyl α-chloro-β-hydroxypropionate by drops, and then the mixture was heated to 130-132°. The resulting α-chloroacrylate was distilled; it was dried and fractionated. We obtained 2.8 g (64%).

B.p. 57-60° (55 mm), n_D^{20} 1.4410.

Found %: Cl 28.85. $C_4H_5O_2Cl$. Calculated %: Cl 29.4.

α-Chloroacrylonitrile. A mixture of 15 g of α-chloro-β-hydroxypropionitrile and 3.8 g of sodium acid sulfate was heated to boiling, upon which 2.2 g of α-chloroacrylonitrile distilled off; it was dried and fractionated.

B.p. 87-89°, n_D^{20} 1.4291, d_4^{20} 1.1038, MR_D 20.40; Calc. 20.27.

According to [5]: b.p. 86-87.5°, n_D^{20} 1.4297.

Phenyl α-chloroacrylate. To a solution of 54.5 g of phenyl-α,β-dichloropropionate in 100 ml of benzene was added a solution of 45 g of triethylamine in 100 ml of benzene. A heavy precipitate of triethylamine hydrochloride formed. After standing two days, the precipitate was filtered off (30.5 g). From the filtrate in a vacuum the benzene was distilled off, and the excess triethylamine and residue were fractionated in the presence of phenyl-β-naphthylamine. After three fractionations we obtained 22 g (49%).

B.p. 94-96° (5 mm), n_D^{20} 1.5325, d_4^{20} 1.2168; MR_D 46.61; Calc. 46.22.

According to [3]: b.p. 91-93° (8 mm), n_D^{20} 1.5808.

Found %: Cl 19.53. $C_9H_7O_2Cl$. Calculated %: Cl 19.45.

SUMMARY

Treatment of methyl acrylate and acrylonitrile with hypochlorite gives the methyl ester and nitrile of α-chlorohydracrylic acid; some of its derivatives were obtained, and we have also described the synthesis of methyl α-chloroacrylate by dehydration of the chlorohydracrylates.

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THERMAL SPLITTING OF TETRAETHYL LEAD, HEXAETHYL DIPLUMBANE AND THEIR ANALOGS

III. REACTION OF HOMOLYTIC SPLITTING OF HEXAETHYL DIPLUMBANE AND HEXAETHYL DISTANNANE

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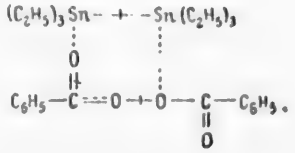
We have previously shown [1, 2] that thermal splitting of tetraethyl lead in the liquid phase occurs with intermediate formation of less ethylated compounds, hexaethyl diplumbane and diethyl lead.

$$(C_2H_5)_4Pb \rightarrow (C_2H_5)_6Pb_2 \rightarrow (C_2H_5)_2Pb \rightarrow Pb$$

There is no doubt that in the course of this complex process there occurs repeated homolytic splitting of the σ-bond. Therefore, for setting up a sufficiently complete and arguable scheme of the splitting, it is necessary to know the path of the homolytic splitting of tetraethyl lead and the intermediate products of its decomposition, and also the role of free radicals in this transformation. From this point of view it is certainly of interest to study the reaction of homolytic splitting of hexaethyl diplumbane and its tin analog, hexaethyl distannane.

In one of our previous studies [3] we showed that hexaethyl distannane reacts smoothly with dibromoethane with formation of triethyl tin bromide and ethylene. We suggested that the reagents formed a transitional cyclic complex which split in a homopolar manner.

It is possible to assume such a cyclic complex also in other reactions of hexaethyl distannane. To test this, we studied the reaction of hexaethyl distannane in benzene solution with compounds which easily split into radicals. We studied benzoyl peroxide and acetylbenzoyl peroxide, the dinitrile of azoisobutyric acid, the cyclohexyl ester of percarbonic acid, nitrosoacetanilide, and lead tetraacetate. All these substances except the dinitrile of azoisobutyric acid react with hexaethyl distannane at room temperature. The reaction of the peroxides occurs most simply of all: in the reaction of benzoyl peroxide with hexaethyl distannane, triethyl tin benzoate is formed; with acetylbenzoyl peroxide, the result is a mixture of triethyl tin benzoate and acetate. Cyclohexyl percarbonate gave triethylcyclohexyl tin. Since these peroxides are not split at ordinary temperature, their easy reaction with the rather stable hexaethyl distannane can be explained by the formation of an unstable intermediate cyclic complex with the following structure:



or another with a four or eight membered ring. In general the reaction is expressed by the following equations.

$$(C_2H_5)_6Sn_2 + (C_6H_5COO)_2 \rightarrow 2(C_2H_5)_3SnOCOC_6H_5 \text{ (I)}$$

$$(C_2H_5)_6Sn_2 + C_6H_5COOOCOCH_3 \rightarrow (C_2H_5)_3SnOCOC_6H_5 + (C_2H_5)_3SnOCOCH_3 \text{ (II)}$$

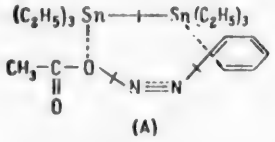
$$(C_2H_5)_6Sn_2 + (C_6H_{11}OCOO)_2 \rightarrow 2(C_2H_5)_3SnOC_6H_{11} + 2CO_2 \text{ (III)}$$

As a side reaction in (I) and (II) was found diethyl tin dibenzoate, probably formed by a disproportionation reaction. Just as simply, but, in distinction from reactions (I)-(III), practically instantaneous, occurs the reaction of hexaethyl distannane with lead tetraacetate:

$$(C_2H_5)_6Sn_2 + Pb(OCOCH_3)_4 \rightarrow 2(C_2H_5)_3SnOCOCH_3 + Pb(OCOCH_3)_2 \text{ (IV)}$$

Hexaethyl diplumbane reacts in a similar way with the above reagents. For example, on mixing benzene solutions of lead tetraacetate and hexaethyl diplumbane, triethyl lead acetate is rapidly formed. It is interesting to note that on long heating of hexaethyl distannane with the dinitrile of azoisobutyric acid in benzene solution there is splitting of the latter with evolution of nitrogen and formation of the dinitrile of tetramethyl succinic acid. The cyanoisopropyl radical does not show any action on hexaethyl distannane.

Much more complex is the reaction of hexaethyl distannane and hexaethyl diplumbane with nitrosoacetanilide in benzene. In spite of the mild conditions of running the reaction (room temperature), there is strong tar formation in both cases. The sole identified reaction products are triethyl tin acetate and, in poorer yield, triethyl lead acetate. In the latter case there is formed a considerable quantity of tetraethyl lead, evidently by a disproportionation reaction. Triethyl phenyl tin or triethyl phenyl lead which could be formed as a result of splitting of the intermediate cyclic complex (A) are not found in the reaction products.



(A)

In all the cases considered above, the solvent (benzene) does not take part in the reaction.

We have shown that when benzene is replaced by carbon tetrachloride, the solvent is no longer inert. Thus, for example, in the reaction of hexaethyl distannane with benzoyl peroxide, besides the normal reaction product, triethyl tin benzoate, there is formed a considerable amount (17.5%) of triethyl tin chloride. It is perfectly clear that the latter can be obtained only from the CCl_4. However, when the analogous experiment is run with acetylbenzoyl peroxide, only the usual products are obtained, triethyl tin acetate and benzoate. The presence of triethyl tin chloride in this case is established only by the characteristic odor of the latter. The participation of CCl_4 in these reactions may be explained on the basis of two assumptions: 1) all three components react simultaneously, 2) two substances react and the compound formed as a result of the reaction reacts further with the third component. The second variant seems the more probable to us. In fact, if CCl_4, benzoyl peroxide (or acetylbenzoyl peroxide), and hexaethyldistannane reacted directly, there should be a definite ratio between the triethyl tin benzoate and chloride. However, experiment shows that in the case of benzoyl peroxide the yield of triethyl tin chloride is 17.5%, while with acetylbenzoyl peroxide only traces of the chloride are formed. Therefore it seems more likely that in CCl_4 there are two parallel and independent reactions. On the one hand, as in benzene solution, the peroxide reacts with hexaethyl distannane. However, at the same time there occurs chlorination of the hexaethyl distannane by carbon tetrachloride, initiated by the peroxide.

In this respect, an analogous reaction can be carried out in the chlorination of mercury organic compounds by carbon tetrachloride, initiated by peroxides [4]. The possibility of the appearance of free radicals in these systems can be confirmed by the initiation of polymerization. For this purpose we used the nitrile of acrylic acid. If to a solution of hexaethyl distannane in acrylonitrile we add a solution of benzoyl peroxide in CCl_4, formation of the polymer is rapid. Under the same conditions in a mixture of benzoyl peroxide, carbon tetrachloride and acrylonitrile, the beginning of polymerization can be established only after 3-4 hours. Finally, acrylonitrile remains practically unchanged in the presence of hexaethyl distannane and CCl_4.

Thus, the suggestion of the initiation of the chlorination reaction because of the presence of benzoyl peroxide and carbon tetrachloride in the mixture seems most likely.

The reaction of hexaethyl distannane is more complex with nitrosoacetanilide in alkyl halide solutions. We noted above that in the reaction of nitrosoacetanilide with hexaethyl distannane in benzene we could not determine the fate of the phenyl residue. However, in carbon tetrachloride solution the reaction of these reagents leads to a quantitative yield of phenyl diazonium chloride. Hence, nitrosoacetanilide in this case reacts in the diazo form and the reaction occurs without evolution of nitrogen with splitting of the N-O bond. Besides phenyl diazonium chloride the reaction mixture contains triethyl tin acetate and chloride.

It is known that hexaethyl distannane with CCl_4 at room temperature does not react, but nitrosoacetanilide and carbon tetrachloride react with formation of phenyl diazonium chloride even in the absence of hexaethyl distannane [5]. It is therefore natural to assume that the formation of triethyl tin chloride is initiated by the reaction of nitrosoacetanilide with carbon tetrachloride.

This effect evidently has a general character, since in solutions in other alkyl halides the formation of triethyl tin halide occurs. The fact that in running the reaction in methyl chloride or ethyl bromide there is no formation of the phenyl diazonium chloride or bromide can be explained by the greater solubility and hence lower stability of these compounds in these alkyl halides as compared to CCl_4.

The duration of the reaction can also act on the yield of phenyldiazonium chloride. In fact, we have already noted that there are indications in the literature of obtaining phenyl diazonium chloride in the reaction of nitrosoacetanilide and CCl_4 [5]. Along this line, Waters [6], repeating this reaction, could not establish the occurrence of these products. Moreover, studying the splitting of nitrosoacetanilide in a number of alkyl halides (especially in ethyl bromide) the author concluded that decomposition was accompanied by evolution of nitrogen and the formation of phenyl radicals which broke off halogen atoms from the solvent. It is known, however, that phenyl radicals which arise from the photochemical splitting of metalloorganic compounds or in the course of the breakdown of benzoyl peroxide by reaction with alkyl halides split off hydrogen and not halogen atoms. Repeating the experiments of Waters with ethyl bromide, but shortening the length of the reaction to one day, we succeeded in isolating phenyl diazonium bromide with a yield of up to 13%.

Analogous results were obtained with the decomposition of nitrosoacetanilide in methyl chloroacetate and benzyl chloride. Also, in all cases we found acetic acid and a small amount of biphenyl in the reaction products. Dimethyl succinate or dibenzyl, which could have been obtained by dimerization of the residues after removal of chlorine from $ClCH_2COOCH_3$ or from $C_6H_5CH_2Cl$, were not found in the reaction products.

Thus, the occurrence of halogenated benzene in the experiments of Waters is evidently more correctly explained not by the appearance in the reaction mixture of kinetically independent phenyl radicals, but by the originally formed phenyl diazonium halide with its later decomposition into nitrogen and benzene halide.

The reactions of nitrosoacetanilide required further work for their explanation.

EXPERIMENTAL

All the experiments with hexaethyl diplumbane and hexaethyl distannane were carried out in a stream of purified, dry hydrogen or in sealed evacuated ampules. In the latter case in an apparatus which consisted of two ampules sealed in the form of the letter H were placed the starting substances. The contents of the ampules were twice frozen and melted in a vacuum to remove oxygen of the air, after which the ampules were sealed and the components of the reaction were mixed.

Reaction of benzoyl peroxide with hexaethyl distannane in benzene. To a solution of 4.12 g (0.01 mole) of hexaethyl distannane in 15 ml of dry benzene was added a solution of 2.42 g (0.01 mole) of benzoyl peroxide in 30 ml of benzene. The mixture stood for three days at room temperature in the dark, after which it was fractionated in a vacuum. We obtained 4.75 g (75.4%) of triethyl tin benzoate. B.p. 120-128° (1 mm), m.p. 78-79° (from ligroin). According to [7]: b.p. 124° at 1 mm, m.p. 80°. A mixed sample with pure triethyl tin benzoate gave no melting point depression.

From the residue after distillation of the triethyl tin benzoate two crystallizations from hexane separated 0.65 g of substances with m.p. 208-209°. A mixed melting point with diethyl tin dibenzoate obtained by a different synthesis gave no depression. The yield of diethyl tin dibenzoate (on the tin) was 7.1%.

Reaction of benzoyl peroxide with hexaethyl distannane in CCl_4. Solutions of 2.00 g (0.00485 mole) of hexaethyl distannane in 15 ml of CCl_4 and 1.18 g (0.00487 mole) of benzoyl peroxide in 40 ml of carbon tetrachloride were mixed in the absence of atmospheric oxygen and allowed to stand at room temperature in the dark for two days: CCl_4 was distilled off at diminished pressure. From the residue we filtered off 0.52 g (44.1%) of unreacted benzoyl peroxide.

The mother liquor was fractionated in a vacuum. We isolated 0.41 g of triethyl tin chloride. Yield (on the tin) 17.5%: b.p. 100-103° (15 mm), nD^{20} 1.5063. According to [8, 9] b.p. 100-101° at 16 mm, nD^{20} 1.5055.

We also obtained 1.15 g (36.2%) of triethyl tin benzoate. B.p. 128-130° (1.5 mm), m.p. 80°, which agreed with the literature [7].

From the residue not fractionated in a vacuum we isolated 0.33 g (8.5% on the tin) of diethyl tin dibenzoate. M.p. 209-210° (from acetone). A mixed sample with a commercial preparation of diethyl tin dibenzoate gave no melting point depression.

Reaction of acetylbenzoyl peroxide with hexaethyl distannane in CCl_4. By the method described above, from 3.18 (0.0077 mole) of hexaethyl distannane and 0.7 g (0.0039 mole) of acetylbenzoyl peroxide in CCl_4 (40 ml) we obtained 0.88 g (21.4% on the tin) of triethyl tin acetate. M.p. 133-134° (from hexane). A mixed sample with the pure substance [10] gave no melting point depression.

We also isolated 1.00 g (19.8%) of triethyl tin benzoate, m.p. 80°, which agreed with the literature [7]. Recrystallization of the residue from acetone gave 0.78 g (12.6% on the tin) of diethyl tin dibenzoate. M.p. 213-214°. A mixed sample with pure substance obtained by a different synthesis gave no depression. The reaction mixture had a strong characteristic odor of triethyl tin chloride, which showed the presence of traces of this in the reaction product.

Reaction of benzoyl peroxide with hexaethyl distannane in CCl_4 in the presence of acrylonitrile. To a mixture of 1.38 g (0.00335 mole) of hexaethyl distannane with 5 ml of freshly distilled, inhibitor-free acrylonitrile at room temperature in the dark was added a solution of 0.41 g (0.0017 mole) of benzoyl peroxide in 5 ml of CCl_4. Polymerization of the acrylonitrile began rapidly.

Under the same conditions in a mixture of 0.41 g of benzoyl peroxide, 5 ml of CCl_4, and 5 ml of acrylonitrile, and also in a mixture of 0.41 g of benzoyl peroxide, 5 ml of benzene, and 5 ml of acrylonitrile, traces of polymer were observed only after 3-4 hours. A mixture of 1.11 g of hexaethyl distannane, 5 ml of CCl_4 and 5 ml of acrylonitrile did not change in the course of two days.

Reaction of hexaethyl distannane with lead tetraacetate. A solution of 1.11 g (0.0025 mole) of lead tetraacetate in 25 ml of dry benzene was added to 1.03 g (0.0025 mole) of hexaethyl distannane. A curdy precipitate slowly formed which contained lead acetate and triethyl tin acetate. The reaction mass was heated to boiling and filtered. From the filtrate on cooling there crystallized 0.84 g (63.6%) of triethyl tin acetate. M.p. 133-134° (from benzene). A mixed sample with pure triethyl tin acetate gave no melting point depression. From the precipitate which was insoluble in boiling benzene we extracted lead acetate with hot water. The water extract was treated with Na_2SO_4. We collected 0.32 g.

Reaction of hexaethyl diplumbane with lead tetraacetate. By a method analogous to that described above, from 2.2 g of lead tetraacetate (0.005 mole) and 2.93 g of hexaethyl diplumbane (0.005 mole) in 30 ml of dry benzene we obtained 0.87 g (49.3%) of triethyl lead acetate. M.p. 158-159° (decomposition, from benzene). The literature [11] gives m.p. 160.4°. A mixed sample with pure triethyl lead acetate gave no melting point depression. From the residue, insoluble in the boiling reaction mixture, hot water extracted lead acetate. In the usual way we secured 0.5 g (33.0%) of $PbSO_4$.

Decomposition of the dinitrile of azoisobutyric acid in the presence of hexaethyl distannane. Equimolecular amounts of hexaethyl distannane (4.12 g) and the dinitrile of azoisobutyric acid (1.64 g) were dissolved in 25 ml of dry benzene. The mixture was boiled for twelve hours, after which the benzene was distilled off. Vacuum distillation gave from the residue 3.1 g (75.3%) of unchanged hexaethyl distannane. B.p. 137-139° (9 mm), nD^{20} 1.5407.

The residue in the Claisen flask was twice recrystallized from alcohol. We obtained 1.1 g (80.0%) of the dinitrile of tetramethyl succinic acid. M.p. 169°. According to [12], m.p. 166-168°. A mixed sample with the pure dinitrile of tetramethyl succinic acid gave no melting point depression.

Reaction of dicyclohexyl percarbonate with hexaethyl distannane. One g of dicyclohexyl percarbonate (0.0035 mole) was mixed with a solution of 1.36 g (0.0035 mole) of hexaethyl distannane in 15 ml of dry benzene and the mixture was kept at room temperature for two days. Fractionation in a vacuum gave 1.62 g (75.9%) of triethylcyclohexyloxy tin. B.p. 120-124° (5 mm), nD^{20} 1.4923.

Found %: Sn 39.43, 39.51. $C_{12}H_{26}OSn$. Calculated %: Sn 38.91.

Preparation of triethylcyclohexyloxy tin. To the alcoholate of cyclohexanol obtained on solution of 1.15 g (0.05 g atom) of sodium in 30 ml of anhydrous cyclohexanol was added with stirring a solution of 12.05 g (0.05 mole) of triethyl tin chloride in 50 ml of dry ether. The mixture was boiled 0.5 hour and allowed to stand over night. Without separating the NaCl the mixture was transferred to a Claisen flask and fractionated in a vacuum. We obtained 5.50 g (36.0%) of triethylcyclohexyloxy tin. B.p. 121-123° (5 mm), nD^{20} 1.4903.

Found %: Sn 39.11, 39.27. $C_{12}H_{26}OSn$. Calculated %: Sn 38.91.

Reaction of nitrosoacetanilide with hexaethyl distannane in benzene. To a solution of 8.66 g (0.022 mole) of hexaethyl distannane in 25 ml of dry benzene with stirring and ice cooling in a stream of hydrogen we added during 0.5 hour 3.47 g (0.021 mole) of nitrosoacetanilide. The mixture was stirred for three hours with cooling by ice water, then left over night at room temperature. During the reaction the mixture took on a cherry color and a crystalline precipitate formed. The benzene was distilled off in a vacuum. Ten ml of hexane was added to the residue. We obtained 4.79 g (43.2% based on the tin) of triethyl tin acetate; m.p. 130-131° (from hexane), which agreed with the literature data [10]. A mixed sample with a commercial form of triethyl tin acetate gave no melting point depression.

The mother liquor after separation of the triethyl tin acetate was fractionated in a vacuum. We could not isolate triethylphenyl tin or any other individual compounds.

Reaction of hexaethyl diplumbane with nitrosoacetanilide. To a solution of 8.40 g (0.014 mole) of hexaethyl diplumbane in 60 ml of dry benzene in a stream of hydrogen we added with stirring and ice cooling during one hour 2.34 g (0.014 mole) of nitrosoacetanilide. The mixture was further cooled for seven hours and left at room temperature over night. The crystalline precipitate was filtered off and washed with ligroin. We obtained 2.22 g (21.7% on the lead) of triethyl lead acetate. M.p. 159-160° (from benzene). According to [11], m.p. 160.4°. The residue after separation of the triethyl lead acetate was steam distilled. The distillate was extracted with ether. In the usual way we isolated from the extract 1.6 g (17.3% on the lead) of tetraethyl lead, b.p. 78-81° (12 mm). It was identified in the form of the monochloroacetate. M.p. 142-143° without depression of the melting point when mixed with the pure product. As in the previous experiment, the chief reaction product was a tarry residue from which individual substances could not be isolated.

Reaction of nitrosoacetanilide with hexaethyl distannane in CCl_4. To a solution of 2.84 g (0.007 mole) of hexaethyl distannane in 25 ml of CCl_4 was added with water cooling and stirring 1.20 g (0.007 mole) of nitrosoacetanilide. After twelve hours we filtered 1.00 g of a crystalline product from the reaction mixture; it was not soluble in boiling hexane, ether, or acetone. The substance exploded without melting. It was easily soluble in water. The water solution decomposed with evolution of nitrogen. At the end of the decomposition the solution gave a positive reaction for phenol (tribromide, m.p. 96°) and the chloride ion. Judging by its properties the crystalline product is phenyl diazonium chloride. Yield quantitative.

The reaction mixture after separation of the phenyl diazonium chloride was evaporated. We separated 0.3 g (8.2%) of triethyl tin acetate, m.p. 133° (twice from hexane). A mixed sample with the pure substance gave no melting point depression.

Distillation of the residue in a vacuum gave a fraction with b.p. 84-104° (15 mm). Yield 1.65 g. The fraction was a complex mixture which contained especially triethyl tin acetate and chloride. The fraction was dissolved in ether and repeatedly shaken with a 20% KOH solution which did not contain chloride ions. The alkaline extract was evaporated and acidified (to Congo) with sulfuric acid free from chloride ions. Then the solution was carefully extracted with ether. After drying, the ether was distilled off with a fractionating column, the residue was dissolved in water and analyzed by titration for content of acetic acid. We found the presence of 0.16 g of CH_3COOH. Hence the fraction contained 0.72 g of triethyl tin acetate. The total yield of product (on the tin) was 28.3%. The acid solution after extraction with ether was analyzed for chloride ion in the usual way. We collected 0.36 g of AgCl. The yield of triethyl tin chloride (on the tin) was 18.5%.

Reaction of nitrosoacetanilide with hexaethyl distannane in methylene chloride. We added 1.64 g (0.01 mole) of nitrosoacetanilide to a cooled, stirred solution of 4.12 g (0.01 mole) of hexaethyl distannane in 25 ml of CH_2Cl_2. The mixture was kept at room temperature for a day. We did not observe a marked amount of phenyl diazonium chloride. The mixture was evaporated, the crystalline product was filtered and recrystallized from hexane. We obtained 1.35 g (25.5% on the tin) of triethyl tin acetate. M.p. 130-131°, which agrees with the literature [10].

Fractionation of the residue in a vacuum gave 2.32 g of a mixture which contained triethyl tin chloride and acetate. B.p. 99-108° (16 mm).

Reaction of nitrosoacetanilide with hexaethyl distannane in ethyl bromide. Under the conditions of the preceding experiment, from 1.64 g (0.01 mole) of nitrosoacetanilide and 4.12 g (0.01 mole) of hexaethyl distannane dissolved in 25 ml of ethyl bromide we obtained 2.7 g (50% on the tin) of triethyl tin acetate. M.p. 130° (from hexane). A mixed sample with pure substance gave no melting point depression. Fractionation of the residue in a vacuum gave 1.35 g (23.5%) of triethyl tin bromide. B.p. 104-108° (15 mm), nD^{20} 1.5263. According to the literature [13], b.p. 105-107° (15 mm), nD^{20} 1.5240.

Phenyl diazonium bromide and triethylphenyl tin were not found in the reaction products.

Decomposition of nitrosoacetanilide in ethyl bromide. In 25 ml of ice cooled ethyl bromide we dissolved 5.0 g (0.031 mole) of nitrosoacetanilide. After four hours the ice bath was removed and the mixture was kept at room temperature for 18 hours. The crystalline precipitate of phenyl diazonium bromide was filtered off and carefully washed with ether. We collected 0.76 g (13.3%) of the substance.

This product dissolved in water with evolution of nitrogen. The water solution gave a positive test for bromide ion and phenol. Tribromophenol, m.p. 96° (from benzene). A mixed sample with pure substance gave no melting point depression.

The reaction mixture after removal of the phenyl diazonium bromide was fractionated. The fraction with b.p. 38-134° was extracted with water. The extract was analyzed by titration for content of acetic acid. We showed the presence of 0.013 mole of CH_3COOH. The tarry residue (1.74 g) was steam distilled. We obtained 0.5 g of a product with m.p. 68-70°. A mixed sample with pure biphenyl showed no melting point depression.

Reaction of nitrosoacetanilide with methyl chloroacetate. Five g (0.031 mole) of nitrosoacetanilide was dissolved in 25 ml of $ClCH_2COOCH_3$ cooled with ice. After 13 hours we filtered off 0.7 g (12.4%) of phenyl diazonium chloride. The filtrate was fractionated. We showed in the usual way the formation of 53.4% of the theoretical amount of acetic acid. We separated from the abundant tarry residue by steam distillation 0.06 g of biphenyl. M.p. 69-70°. A mixed sample gave no melting point depression. Dimethyl esters of succinic or fumaric acids were not found among the reaction products. The yield of phenyl diazonium chloride became minimal (trace) if in the course of a day in 25 ml of ice cooled $ClCH_2COOCH_3$ was dissolved 10.8 g of nitrosoacetanilide and the mixture was kept at room temperature for two days.

Decomposition of nitrosoacetanilide in benzyl chloride. In 25 ml of benzyl chloride with ice cooling we dissolved 11.55 g (0.07 mole) of nitrosoacetanilide in the course of day. After 12 hours we filtered off 1.6 g (12.2%) of phenyl diazonium chloride. The filtrate was fractionated. We isolated 1.7 g (40.1%) of acetic acid; b.p. 117-121°, nD^{20} 1.3754. From the tarry residue steam distillation gave 0.1 g of biphenyl. M.p. 70°. A mixed sample with pure substance gave no melting point depression. No dibenzyl or stilbene were found among the reaction products.

SUMMARY

1. Hexaethyl distannane and hexaethyl diplumbane are split homolytically at the metal-metal bond in benzene solution at ordinary temperature when unstable organic compounds act on them: benzoyl and acetylbenzoyl peroxides, cyclohexyl percarbonate, nitrosoacetanilide, and lead tetraacetate. The cyanoisopropyl radical which is formed in the splitting of the dinitrile of azoisobutyric acid shows no analogous action. It is suggested that the reaction occurs with intermediate formation of cyclic complexes which are split homolytically.

2. We have shown that in the reaction of hexaethyl distannane with the compounds mentioned above in carbon tetrachloride solution the solvent shares in the reaction so that triethyl tin chloride is formed. The appearance of this product along with the ordinary reaction products is initiated by the reaction of CCl_4 with unstable compounds. The formation of free radicals is confirmed by the initiation of a polymerization reaction for acrylonitrile.

3. Nitrosoacetanilide at ordinary temperatures reacts with carbon tetrachloride, ethyl bromide, benzyl chloride, and methyl chloroacetate with formation of phenyl diazonium chloride and bromide, acetic acid, and traces of biphenyl.

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THE PROBLEM OF THE REACTIVITY OF NITRILES OF DIBASIC ALIPHATIC ACIDS

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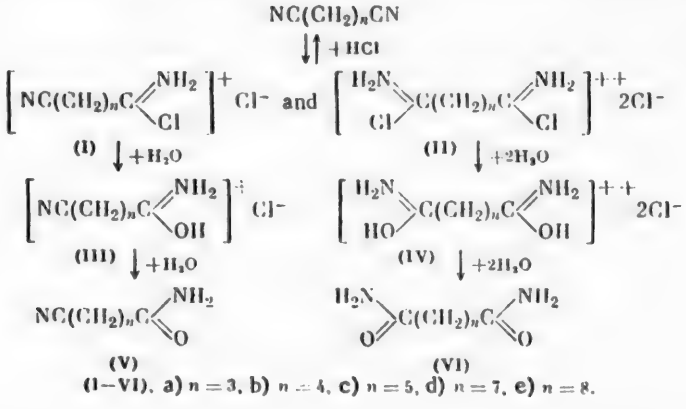
It has recently been shown [1] that in the hydrochlorination of adiponitrile the first two molecules of hydrogen chloride are selectively added to one nitrile group. The resulting compound is evidently δ-cyanovaleric acid iminochloride hydrochloride. In continuation of the hydrochlorination there is formed the adipic acid diiminochloride dihydrochloride. From both iminochloride hydrochlorides by treatment with water or alcohol there are obtained almost quantitative yields of the corresponding hydrochlorides of the amides or iminoesters [1, 2]. It was also found that adiponitrile forms a very stable molecular compound with δ-cyanovaleric acid amide and iminoester hydrochlorides.

Hydrogenation of adiponitrile in the presence of skeletal nickel as a catalyst gives a high yield of ε-aminocapronitrile [3]. In amidoximation [4] of adiponitrile under definite conditions only one functional group reacts, and the second functional group reacts with hydroxylamine only at higher temperature. In the case of amidoximation of sebacic nitrile conditions could not be found in which one nitrile group would react selectively.

In order to obtain new data needed to explain the nature of the selective reactivity of one nitrile group in adiponitrile we studied the reaction with hydrogen chloride and water of other dinitriles of the same homologous series: glutaronitrile, pimelonitrile, azelaonitrile, and sebaconitrile. At the same time we have tried to work out suitable preparative methods for obtaining and isolating from the reaction mixtures the diiminohydrins and amides of dicarboxylic and ω-cyanocarboxylic acids.

In order to obtain these compounds, the dinitriles, dissolved in ether, were treated with hydrogen chloride. To the homogeneous solution of the hydrochlorination products (I, II) we added water calculated at 1 mole per 2 moles HCl, as a result of which the iminohydrin hydrochlorides (III and IV) precipitated, and were hydrolyzed by excess water into the corresponding amides of ω-cyanocarboxylic acids (V) and diamides (VI) [1, 5].



(I–VI). a) $n = 3$, b) $n = 4$, c) $n = 5$, d) $n = 7$, e) $n = 8$.

Reactions of Dinitriles with Hydrogen Chloride and Water (0.05 mole of dinitrile in 20 ml of ether)

Expt. No.	Starting dinitrile	Hydrogen chloride (in moles)	Water (in moles)	Duration of crystallization (in days)	Obtained on hydrolysis: nitrile amides (V) (in g)	nitrile amides (V) (in % of theory on dinitrile)	diamides (VI) (in g)	diamides (VI) (in % of theory on dinitrile)
1	Glutaronitrile	0.2	0.1	3	—	—	6.2	97
2	The same	0.1	0.05	2	2.6	46.5	2.0	31
3	»	0.05	0.025	12	Trace	—	Trace	—
4	Pimelonitrile	0.2	0.1	6	—	—	7.6	96.5
5	The same	0.1	0.05	8	3.3	47	2.2	28
6	»	0.05	0.025	12	1.6	23	0.4	5
7	Azelaonitrile	0.2	0.1	5	—	—	9.0	97
8	The same	0.1	0.05	7	3.9	46.5	2.8	30
9	»	0.05	0.025	10	2.3	27	0.6	6
10	Sebaconitrile	0.2	0.1	5	—	—	9.8	98
11	The same	0.15	0.075	7	2.9	32	5.3	53
12	»	0.1	0.05	6	4.0	44	2.5	25
13	»	0.075	0.037	7	2.0	23	0.7	7
14	»	0.05	0.025	8	2.2	24	0.6	6

As the data in the table show, at mole ratios between dinitrile, hydrogen chloride, and water of 1:4:2 (experiments 1, 4, 7, and 10) in all cases with comparative ease and almost quantitative yields we obtained diimino hydrochlorides (IV) and diamides (VI). In order to hasten considerably the formation of substance (IV) we could use a stoichiometric excess of HCl (see experimental part). At ratios between the starting components of 1:2:1 (experiments 2, 5, 6, and 12), that is, under conditions in which adiponitrile is quantitatively converted into δ-cyanovaleric iminohydrin hydrochloride (IIIb), we obtained mixtures of chlorides (III) and (IV). Under these conditions we found the maximum absolute yield of nitrile amides (Va, c-e) in experiments 11-14. Experiments 3, 6, 9, and 14 showed that γ-cyanobutyric iminohydrin hydrochloride (IIIa), ε-cyanocaproic derivative (IIIc), ω-cyanocaprylic derivative (IIId), and ω-cyanopelargonic derivative (IIIe), in distinction from (IIIb) do not form solid molecular compounds with the corresponding dinitriles.

Thus the selective reactivity of one nitrile group is absent in dinitriles with a longer or shorter carbon chain than in adiponitrile. In the homologous series of aliphatic dinitriles, this effect, whose cause is still unclear, is specific for adiponitrile. If the specific reactivity of adiponitrile were dependent on any intermolecular reaction, then the outer dinitriles should react like adiponitrile. Therefore we can assume that the selective reactivity is connected with the nonlinear structure of adiponitrile and δ-cyanovaleric iminochloride hydrochloride (Ib), with the formation of an unstable ring due to reaction of the nitrile nitrogen with the methylene group in the α-position with respect to the second functional group. The formation of an analogous six-membered ring by the molecule of glutaronitrile is excluded since in this case the α-hydrogen atom is not sterically available for the nitrogen atom of the other nitrile group. In the case of pimelonitrile, evidently because in eight-membered and similar rings there must be a considerable number of energetically unfavorable conformations, there must occur relatively large torsional forces (Pitzer forces) [6].

We should remember that a position in some degree analogous to that occupied by adiponitrile in the series of aliphatic dinitriles is held by adipic aldehyde in the series of aliphatic dialdehydes. Adipic aldehyde more easily than the other aldehydes undergoes intramolecular aldol condensation. Among the dialdehydes glutaric and succinic aldehydes, because of the absence of the corresponding steric factors, do not undergo this reaction at all.

EXPERIMENTAL

Starting products. For the preparation of glutaronitrile we started from 1,3-dibromopropane [8]. We placed 150 g of allyl bromide in a quartz reactor fitted with a reflux condenser and saturated it with hydrogen bromide at 35-40°. The reactor was irradiated with a mercury-quartz lamp PRK-2 at a distance of 20 cm. After four hours the weight of the reaction mass had increased to 242 g, after which the resulting product was neutralized with 5% soda solution, washed with water, dried over sodium sulfate, and vacuum distilled. We obtained 168 g (67%) of 1,3-dibromopropane, b.p. 76-76.5° (50 mm).

We placed 137 g of 1,3-dibromopropane in 220 ml of alcohol in a reactor fitted with a reflux condenser and dropping funnel. The reactor was heated on a water bath to boiling of the alcohol and during 40 minutes we added a saturated aqueous solution of 95 g of potassium cyanide and continued heating for two hours more. The reaction product was treated as described in the literature [9]. We obtained 45 g (70%) of glutaronitrile with b.p. 131-135° (10 mm) d_4^{20} 0.994, nD^{20} 1.4360.

In this study we used sebaconitrile obtained previously [4]. Azelaonitrile (d_4^{20} 0.935, nD^{20} 1.4452) and pimelonitrile (d_4^{20} 0.949, nD^{20} 1.4424) were synthesized like sebaconitrile from azelaic and pimelic acids [4] with yields of 82 and 83% respectively. The starting pimelic acid was obtained from salicylic acid [10]. The constants of the resulting nitriles agreed with the literature.

Obtaining the diiminohydrin dihydrochlorides (IV) and the diamides (VI).

Sebacic amide (exp. 10). Into a mixture of 8.2 g (0.05 mole) of sebaconitrile and 20 ml of dry ether with cooling to 0° and stirring was passed 7.3 g (0.2 mole) of hydrogen chloride. After keeping in the cold for four hours we added to the mixture 1.8 g (0.1 mole) of water. After five days the precipitate which came down in the cold was filtered off, washed with dry ether, and dried in a desiccator over calcium chloride. We obtained 13.8 g of substance (IV e) with m.p. 136° (decomposition).

Found %: Cl 25.0; N 10.5. $C_{10}H_{22}O_2N_2Cl_2$. Calculated %: Cl 26.0; N 10.25.

Ten g of substance (IVe) was hydrolyzed with 30 ml of water and neutralized to methyl orange with 10% sodium hydroxide solution. The resulting precipitate was filtered off, washed with water, and dried. We obtained 7.15 g (98% calculated on the starting nitrile) of sebacic amide (VIe) with m.p. 209-210° (from dimethylformamide); the literature gives m.p. 208-210° [11].

At a molar ratio of sebaconitrile to hydrogen chloride 1:8 the time of crystallization of (IVe) was shortened to one day.

Glutaric amide (expt. 1). A homogeneous solution obtained after hydrolysis of the product of the reaction of glutaronitrile with hydrogen chloride and water was neutralized with 10% sodium hydroxide and evaporated dry. The residue was extracted with boiling dimethylformamide in a continuous extractor for three hours. On cooling, glutaric amide (VIa) precipitated from the extract. Ether precipitated a further amount of (VIa) from the mother liquor, m.p. 175° (from a mixture of dimethylformamide and ether); the literature gives m.p. 174-175° [12].

Pimelic amide (expt. 4) was obtained like substance (VIa), m.p. 174-175° (from alcohol); the literature gives 174-175° [13].

Azelaic amide (expt. 7). From 7.5 g (0.05 mole) of azelaonitrile under conditions like those described for the preparation of (IVe) we obtained 12.95 g of azelaic acid diiminohydrin dihydrochloride (IVd) with m.p. 130° (decomposition).

Found %: Cl 26.5; N 10.7. $C_9H_{20}O_2N_2Cl_2$. Calculated %: Cl 27.0; N 10.8.

By hydrolysis of (IVd) we obtained (VId), m.p. 174° (from water); the literature gives m.p. 175° [14].

Isolation of the amides of ω-cyanocarboxylic acids (V) from their mixtures with the diamides. The mixture of iminohydrin hydrochlorides of the ω-cyanocarboxylic acids (III) and diiminohydrin dihydrochlorides of the corresponding dicarboxylic acids (IV) (expts. 2, 3, 5,6,8,9, 11-14) was obtained by the method described for (IVe).

ω-Cyanopelargonic amide (expt. 12). Six g of a mixture of chlorides (IIIe) and (IVe) was hydrolyzed with 20 ml of water, neutralized with 10% sodium hydroxide to methyl orange, and from the heterogeneous mixture, heated to boiling, was filtered 0.6 g of sebacic amide. The filtrate was evaporated dry and the residue was extracted successively with boiling ethyl acetate and dimethylformamide in a continuous extractor. When the ethyl acetate was evaporated we isolated 3.0 g of ω-cyanopelargonic amide (Ve); yield 44% (on the dinitrile), m.p. 74-75° (from water); the literature gives m.p. 74-75° [15].

From dimethylformamide ether precipitated a further amount of sebacic amide. In all we obtained 1.9 g (25%) of (VIe), identical with that obtained in expt. 10.

In an analogous way we separated from the corresponding diamides the following nitrileamides: γ-cyanobutyric amide (Va) (expt. 2), m.p. 69-70° (from a mixture of ethyl acetate and ether; the literature gives m.p. 69-70° [16]; ε-cyanocaproic amide (Vc) (expt. 5), m.p. 89-91° (from ethyl acetate); the literature gives m.p. 89-91° [17]; ω-cyanocaprylic amide (Vd) (expt. 8), m.p. 83-84° (from ethyl acetate); the literature gives m.p. 84-85° [18]. For the extraction of substance (Va) instead of ethyl acetate we used acetonitrile. When we cooled the acetonitrile a small amount of glutaric amide precipitated and was filtered off. γ-Cyanobutyric amide was isolated by evaporating the filtrate.

SUMMARY

1. We have studied the reaction of aliphatic dinitriles with hydrogen chloride and water. We have worked out a method for obtaining the diamides of dibasic acids and the amides of ω-cyanocarboxylic acids from the corresponding dinitriles.

2. We have showed that in the hydrolysis of the dinitriles of glutaric, pimelic, azelaic, and sebacic acids selective binding of the HCl with one nitrile groups does not occur. Here there is basis for suggesting that the previously described selective reactivity of the nitrile group in the adiponitrile is related to the nonlinear structure of its molecule.

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ETHERS OF ACETYLENE ALCOHOLS AND GLYCOLS AND THEIR RELATION TO AMMONIACAL SOLUTIONS OF SILVER OXIDE

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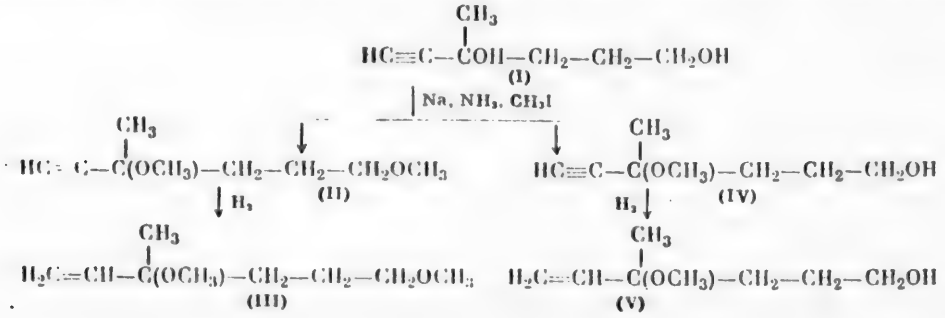
We showed previously that some acetylene glycols which contain free acetylene hydrogen, the β-glycol 3,5-dimethyl-1-hexyn-3,5-diol [1] and the γ-glycol 3-methyl-1-hexyn-3,6-diol [2] under ordinary conditions do not form a precipitate under the action of an ammoniacal solution of silver oxide; a precipitate of acetylenic silver appears only when the reaction mixture is heated. On the other hand, we have studied ethers of dimethylacetylenyl carbinol and have shown [2] that the ethyl ether of this alcohol forms a precipitate of acetylenic silver as easily as does the carbinol, while the benzyl ether of dimethylacetylenyl carbinol does not react with ammoniacal silver oxide even when heated to boiling. We tried to connect such peculiar relationships with the silver reagent to the presence in these compounds of intermolecular acetylenic hydrogen bonds [3], but such bonds were observed not only in those compounds which did not give a precipitate of acetylenic silver, but also in dimethylacetylenyl carbinol and its ethyl ether, and in a series of other acetylenic oxygen-containing derivatives which react easily with ammoniacal solutions of silver oxide.

Since the experimental material on this question is still very scanty, all new data in this field present considerable interest.

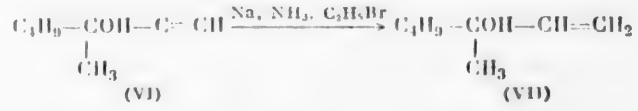
Therefore we studied ethers of 3-methyl-1-hexyn-3,6-diol and 3,5-dimethyl-1-hexyn-3,4-diol and tried to synthesize the methylethyl- and methyl-n-butylacetylenyl carbinols.

The synthesis of the ethers of the alcohols and glycols was carried out by reaction of the latter with sodium and alkyl halides in liquid ammonia. In running the reaction of 3-methyl-1-hexyn-3,6-diol with sodium and methyl iodide to obtain the dimethyl ether of this glycol we obtained both the mono- and diether, but along with this there occurred partial formation of the ethylenic ethers due to reduction of the triple bond by the evolved hydrogen. Although we were not able to separate fully the four reaction products formed, yet the data of the analyses and the photographs of the infrared spectra allow us to assume that the reaction goes as follows.



In running the reaction under the same conditions, but with 1 g-atom of sodium, we obtained the same mixture of products, and also some unreacted starting glycol. Neither of the ethers gave a precipitate of acetylenic silver even when heated.

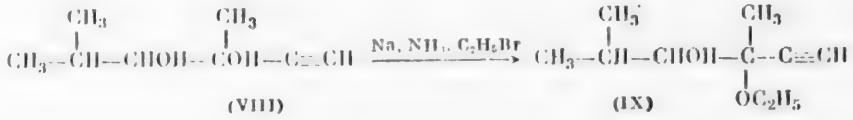
The above reaction scheme is assumed, since we cannot say whether there is reduction of the triple bond in the formation of the ethers or whether it is already reduced in the starting glycol. The latter assumption can be made on the basis of results which we obtained in studying the reaction of methylbutylacetylenyl carbinol and methylethylacetylenyl carbinol with sodium and ethyl bromide in liquid ammonia. Under these conditions, ethers are usually not obtained; methylbutylacetylenyl carbinol (VI) is completely reduced, with formation of methylbutylvinyl carbinol (VII), while methylethylacetylenyl carbinol is only partly hydrogenated to methylethylvinyl carbinol.



(VI) (VII)

The structure of methylbutylvinyl carbinol (VII) was confirmed by its oxidation, as a result of which we obtained methylbutyl ketone and methylbutylglycolic acid, by photographs of the infrared spectrum, and by the results of the hydrogenation in which one molecule of hydrogen was added. In the infrared spectrum of the product obtained from methylethylacetylenyl carbinol we found absorption bands of the vinyl group ((3100 cm^{-1}) [4] and acetylenic bonds (3333 cm^{-1} and 2101 cm^{-1} [5]) (LiF prism).

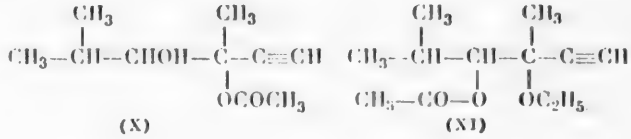
In the reaction of the acetylenic α-glycol 3,5-dimethyl-1-hexyn-3,4-diol (VIII) with sodium and ethyl bromide in liquid ammonia, reduction of the triple bond was not found. As a result of the reaction we obtained the monoether, 3,5-dimethyl-3-ethoxy-1-hexyn-4-ol (IX); part of the glycol was recovered.



(VIII) (IX)

When ether (IX) was heated with a solution of alkali, its decomposition with evolution of acetylene did not occur; this confirmed that the ethoxy group was on the tertiary carbon atom. The structure of the ether was also confirmed by infrared spectrum photographs.

Ether (IX) reacted with ammoniacal silver oxide at room temperature, but only on standing. In the same way ammoniacal silver oxide also reacted with the monoacetyl derivative of glycol (X) and with 3,5-dimethyl-3-ethoxy-4-acetoxy-1-hexyne (XI).

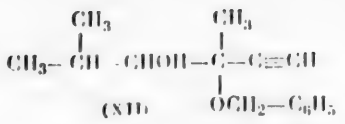


(X) (XI)

Ether (X) was not decomposed with evolution of acetylene under the influence of alkali; this shows that the ether portion is found on the tertiary carbon atom. For both ethers (X) and (XI) we took infrared spectra. As for the benzyl ether of glycol (XII), this does not react with ammoniacal silver oxide solution either at room temperature or with heating.

The benzoxy group in this ether is also on the tertiary carbon atom. The presence of the group $-C\equiv CH$ was confirmed spectroscopically.

Thus, the reaction of acetylenic alcohols and glycols with sodium and alkyl halides in liquid ammonia can lead in one of two directions: 1) formation of ethers, on which, in the case of glycols, the hydroxyl group next to the triple bond reacts, and 2) hydrogenation of the triple bond to an ethylenic one.



(XIII)

In some cases, both these reactions occur. As to the ability of the ethylenic hydrogen to be replaced by silver, in the case of glycol (I), which under ordinary conditions does not give acetylenic silver, its ethers also do not give this precipitate; in the case of glycol (VIII), which forms an acetylenide, its ethyl ether and its mono- and ethoxyacetate also form this precipitate in distinction from the benzyl ether of glycol (VIII), which (like the benzyl ether of dimethylacetylenyl carbinol) does not react with the silver reagent even when heated.

EXPERIMENTAL

O. V. Sergievskaya

Reaction of 3-methyl-1-hexyn-3,6-diol with sodium and methyl iodide in liquid ammonia.

Obtaining the diether. Fifty g of glycol (I) was dissolved in anhydrous ether and slowly poured into liquid ammonia, after which 17 g of metallic sodium in pieces were added (slightly less than two moles). The first mole of sodium reacted so fast that its solution in liquid ammonia did not acquire a blue color. The second mole reacted considerably more slowly, the solution turned blue and decolorized slowly. When the solution had acquired a stable blue color, we added 50 ml of methyl iodide, and the reaction occurred very violently. After evaporation, the reaction mixture was decomposed with a small amount of water, and solution was extracted with ether by hand and in a Soxhlet apparatus. After drying and removal of the ether, the residue was repeatedly fractionated; however, we could not isolate completely pure mono- and diethers. We isolated two fractions: the 1st with b.p. 64-66.5° (8 mm), 20 g, which in the methoxy content was close to the diether, and the 2nd with b.p. 74-76.5° (8 mm), 17 g, which in content of methoxy groups was like the monoether. We also isolated 6 g of unreacted starting glycol.

1st fraction. B.p. 64-66.5°, nD^{20} 1.4340, d_4^{20} 0.8915, MR_D 45.57. $C_9H_{16}O_2F$. Calculated MR_D 45.05. MR_D 46.15. $C_9H_{18}O_2F$. Calculated MR_D 46.58.

Found %: C 69.60; 69.45; H 11.04; 11.46; OCH_3 36.86; 37.12, H_{act} 0.11, 0.15. $C_9H_{16}O_2$. Calculated %: C 69.23; H 10.25; OCH_3 39.75. $C_9H_{18}O_2$. Calculated %: C 68.35; H 11.39; OCH_3 39.23.

2nd fraction. B.p. 74-76.5° (8 mm), nD^{20} 1.4449, d_4^{20} 0.9173. MR_D 41.20. $C_8H_{14}O_2F$. Calculated 40.31. MR_D 41.78. $C_8H_{16}O_2F$. Calculated 41.85.

Found %: C 67.05; H 11.32; OCH_3 23.23; 22.94; OH 10.74; 10.91. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.87; OCH_3 21.83; OH 11.97. $C_8H_{16}O_2$. Calculated %: C 66.66; H 11.11; OCH_3 21.53; OH 11.81.

For both fractions we took the infrared spectra (NaCl prism). We noted an intense absorption band answering the valence oscillation of a = CH group (2100 and 2075 cm^{-1}) [5], and a valence oscillation of an unconjugated double bond (1650 and 1645 cm^{-1}) [6], and also "overtone" deformation oscillation of hydrogen bonds in the group $=CH_2$ (1830 and 1820 cm^{-1}) [7].

L. N. Il'ina

Methylbutylacetylenyl carbinol was obtained by the process of Favorskii.

B.p. 49-50° (5 mm), nD^{20} 1.4410, d_4^{20} 0.8587, MR_D 38.75. $C_8H_{14}OF$. Calculated 38.76.

Literature [8] gives: b.p. 63° (12 mm), nD^{14} 1.4390, d_4^{14} 0.860.

Reaction of methylbutylacetylenyl carbinol and methylethylacetylenyl carbinol with sodium and ethyl bromide in liquid ammonia. Ten g of methylbutylacetylenyl carbinol was carefully poured into liquid ammonia in a wide tube cooled to -35°, and then 1.8 g of sodium was added (small pieces). When the sodium had all reacted, we added 9 g of ethyl bromide. The ammonia was removed by evaporation, anhydrous ether was added and the solution was filtered from the precipitate of NaBr, then the ether was distilled off and the residue was fractionated. We obtained 6 g of methylbutylvinyl carbinol.

B.p. 153-155°, nD^{20} 1.4320, d_4^{20} 0.8297, MR_D 40.01, $C_8H_{16}OF$. Calculated 39.99.

Found %: C 74.94, 74.87; H 12.20, 12.50; OH 12.70, 13.42. M 124. $C_8H_{16}O$. Calculated %: C 75.00; H 12.50; OH 13.28. M 128.

Oxidation of methylbutylvinyl carbinol. In the oxidation of 10 g of the alcohol we used 28.5 g of potassium permanganate. From the neutral oxidation product we obtained a 2,4-dinitrophenylhydrazone of methylbutyl ketone with m.p. 104° [9].

Found %: N 20.28, 20.42. $C_{12}H_{16}O_4N_4$. Calculated %: N 20.00.

The acid obtained in the oxidation was converted to the ammonium salt and treated with concentrated silver nitrate solution.

Found %: Ag 40.63. $C_7H_{13}O_3Ag$. Calculated %: Ag 41.07.

In the hydrogenation of methylbutylvinyl carbinol over platinum black 112% of the hydrogen was absorbed calculated for the double bond.

In the infrared spectrum were absorption bands for the vinyl group (3022 cm^{-1} and 3104 cm^{-1}) and for hydroxyl added by a hydrogen bond (3419 cm^{-1}) [10].

Methylethylacetylenyl carbinol was obtained by the method of Favorskii; its constants agreed with the literature data. Its reaction with sodium and ethyl bromide was carried out under conditions described above. B.p. 107-110°, nD^{20} 1.4202, d_4^{20} 0.8228, MR_D 30.74. $C_6H_{12}OF$. Calculated 30.97.

In the infrared spectrum we found a maximum at 3100 cm^{-1} (CH_2 group) and maxima at 3333 and 2101 cm^{-1} which come from the HC ≡ C–R group.

Hsu Ting-yu

Reaction of 3,5-dimethyl-1-hexyn-3,4-diol with sodium and ethyl bromide in liquid ammonia. The reaction was carried out under the conditions described above for 3-methyl-1-hexyn-3,6-diol. Here part of the glycol (4 out of 28 g) was recovered unchanged; the ether, 3,5-dimethyl-3-ethoxy-1-hexyn-4-ol, was obtained in the amount of 18 g (64%).

B.p. 88-89° (22 mm), nD^{20} 1.4422, d_4^{20} 0.9056, MR_D 49.68. $C_{10}H_{18}O_2F$. Calculated 49.55.

Found %: C 70.79; 70.60; H 10.42; 10.70; ash H_{act} 1.06; 1.06. M 167, $C_{10}H_{18}O_2$. Calculated %: C 70.58; H 10.58; ash H_{act} 1. M 170.

The substance reacted very slowly with an ammoniacal solution of silver oxide and was not decomposed by heating with an alkali solution.

In the infrared spectrum taken in the regions 2916-3644 and 1996-2302 cm^{-1} (LiF prism) we found maxima at 3300 and 2110 cm^{-1} which indicate the presence of the group –C≡CH, and at 3486 cm^{-1}, showing the presence of a hydroxyl group.

Reaction of 3,5-dimethyl-1-hexyn-3,4-diol with acetic anhydride. Eighteen g of glycol, 26 g of acetic anhydride, and 1 g of potassium acetate were heated for 18 hours on a boiling water bath, then the acetic acid and anhydride were distilled off up to 142°; the residue was fractionated in a vacuum at 22 mm. We obtained 15 g (65%) of the glycol monoether.

B.p. 121-123°, nD^{20} 1.4461, d_4^{20} 1.0130, MR_D 48.44. $C_6H_{16}O_3F$. Calculated 48.14.

Found %: C 65.15; 65.30; H 8.71; 8.73. ash H_{act} 1.05; 1.06. M 173. $C_6H_{16}O_3$. Calculated %: C 65.22; H 8.69. ash H_{act} 1. M 184.

In the infrared spectrum taken with a LiF prism we found frequencies of 3300, 2116, and 3487 cm^{-1}, which indicated the presence of the –C≡CH and hydroxyl groups.

Reaction of 3,5-dimethyl-3-ethoxy-1-hexyn-4-ol with acetic anhydride. The reaction was carried out under the conditions of the preceding experiment. Yield of ethoxyacetate 66%.

B.p. 96-100° (14 mm), n_D^{20} 1.4360, d_4^{20} 0.9448, MR_D 58.65. $C_{12}H_{20}O_3F$. Calculated 59.01.

Found %: C 67.32, 67.44; H 9.78, 9.57. M 206. $C_{12}H_{20}O_3$. Calculated %: C 67.65; H 9.85. M 212.

In the infrared spectrum taken with a LiF prism we found absorption bands at 3300 and 2111 cm^{-1}, characteristic for a $-C \equiv CH$ group.

In the hydrogenation 100% hydrogen was absorbed, calculated on the triple bond.

Reaction of 3,5-dimethyl-1-hexyn-3,4-diol with sodium and benzyl chloride in liquid ammonia. The reaction was carried out under the conditions described for the reaction of this glycol with sodium and ethyl bromide in liquid ammonia. The yield of benzyl ether of the glycol was 35%. Part of the glycol was recovered unchanged.

B.p. 159-161° (22 mm), nD^{20} 1.5064, d_4^{20} 1.0025, MR_D 68.73. $C_{15}H_{20}O_2F_3F$. Calculated 69.14.

Found %: C 76.43; 76.52; H 9.10; 9.05. ash H_{act} 1.03, 1.06; M 220. $C_{15}H_{20}O_2$. Calculated %: C 76.57; H 9.01. ash H_{act} 1.0; M 221.

The presence in the molecule of the benzyl ether of acetylenic hydrogen and hydroxyl groups was confirmed by the infrared spectrum: maxima at 3330 and 2265 cm^{-1} ($-C \equiv CH$) and 2112 cm^{-1} (OH).

SUMMARY

1. We have obtained a series of ethers of acetylenic glycols which contain unsubstituted acetylenic hydrogen – 3-methyl-1-hexyn-3,6-diol and 3,5-dimethyl-1-hexyn-3,4-diol.

2. We have shown that in obtaining mono- and dimethyl ethers of 3-methyl-1-hexyn-3,6-diol, in addition to the acetylenic ethers there are formed ethers with a double bond.

3. We have shown that in attempts to synthesize ethyl ethers of methylbutylacetylenyl carbinol and methylethylacetylenyl carbinol there occurs only reduction of these alcohols to alcohols of the ethylenic series.

4. We have shown that the methyl ether of 3-methyl-1-hexyn-3,6-diol and the benzyl ether of 3,5-dimethyl-1-hexyn-3,4-diol do not react with an ammoniacal solution of silver oxide even with heating, while the ethyl and acetyl derivatives of this glycol, and also the corresponding ethoxyacetate, give a precipitate of acetylenyl silver.

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SYNTHESIS AND STUDY OF THE TRANSFORMATIONS OF ACETYLENE α-GLYCOLS WITH FREE ACETYLENIC HYDROGEN.

IV. SYNTHESIS OF TRIMETHYL-ACETYLENYL-ETHYLENE GLYCOL AND 3,4-DIMETHYL-1-HEXYN-3,4-DIOL AND THEIR TRANSFORMATIONS UNDER THE INFLUENCE OF SULFURIC ACID INTO SUBSTITUTED TETRAHYDROFURANONES

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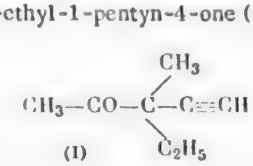
In a preceding communication [1] we have shown that secondary-tertiary acetylene α-glycols, methylacetylenyl isopropyl ethylene glycol and methylacetylenyl-n-propyl ethylene glycol when treated with concentrated sulfuric acid at -10° are converted into a tautomeric mixture of the corresponding substituted tetrahydrofuranones and their enols. Under the influence of alkaline agents these heterocyclic compounds are split into ethylisopropyl- and ethylpropyl ketones and ketene, which is further hydrolyzed into acetic acid.

On the other hand, A. E. Favorskii and A. S. Onishchenko [2] in treating a ditertiary acetylenic glycol, trimethyl acetylenyl ethylene glycol, with sulfuric acid under the same conditions obtained a product of a pinacoline rearrangement and following hydration, a β-ketone, dimethylacetyl acetone, and no other products were isolated.

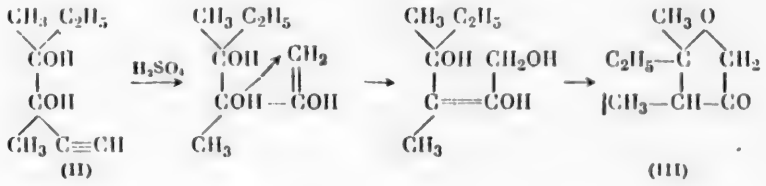
In this connection we decided to study how a close homolog of trimethyl acetylenyl carbinol, 3,4-dimethyl-1-hexyn-3,4-diol (II) would be transformed under the influence of sulfuric acid. In order to obtain this glycol we first synthesized methyl-ethyl-acetylenyl carbinol by the method of A. E. Favorskii and this was then hydrated by the method of M. G. Kucherov. The resulting methyl-ethyl-acetyl carbinol was transformed into the desired glycol. This synthesis was first carried out by the method of A. E. Favorskii and A. S. Onishchenko [3] by condensation of the ketoalcohol with acetylene in the presence of potassium hydroxide; we thus obtained the erythritol 3,4,7,8-tetramethyl-5-decyn-3,4,7,8-tetraol, and some glycol. When distilled, the erythritol decomposed, with formation of glycol. Since the yield of glycol by this process was not good enough, we decided to synthesize it by the action of sodium acetylide on the ketoalcohol in liquid ammonia; by this process the glycol was obtained with a yield of 80-85%. The reaction of the glycol with concentrated sulfuric acid was carried out at -10 to -15°. Distillation of the resulting products gave two fractions; the first with b.p. 45-48° (34 mm), 14%; the second with b.p. 86-87° (43 mm), 40-45%. The first fraction was the product of the pinacoline rearrangement, the acetylenyl ketone, 3-methyl-3-ethyl-1-pentyn-4-one (I).



(I)

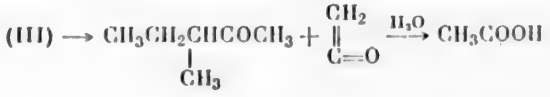
Since this ketone was obtained by us in only one of the experiments in an amount of 1.37 g, we could not determine its structure rigorously; but this formula seems most probable to us since of the two hydroxyl groups of the glycol the more mobile is the one which is fixed to the acetylene residue and when the radicals shift the acetylene group is formed preferentially before other acyl groups. The ketone was converted to the 2,4-dinitrophenylhydrazone, which was completely analyzed. Attempts to obtain the acetylenyl ketone by heating the glycol with 10 and 20% sulfuric acid did not succeed; the glycol was recovered completely.

The second fraction was treated with a solution of potassium permanganate to free it from unsaturated impurities. The presence of a carbonyl group in it was confirmed by the formation of a 2,4-dinitrophenylhydrazone, and also from a photograph of the infrared spectrum with a NaCl prism. The maximum at 1717 cm^{-1} shows the presence of a carbonyl, the maximum at 1058-1106 cm^{-1}, the presence of an ether link. The spectrum confirmed the cyclic nature of this tetrahydrofuranone [4]; in distinction from the tetrahydrofuranones obtained before, this ketone was not enolized. Its formation can be represented as follows.



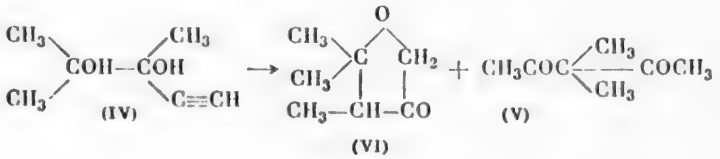
(II) (III)

2,3-Dimethyl-2-ethyl-4-ketotetrahydrofuran (III) was treated with a 30% solution of alkali, and in distinction from the other enols studied 20% alkali did not act on it. As a result of this reaction we obtained methyl sec-butyl ketone and acetic acid. Thus in splitting the tetrahydrofuranone (III) there was a shift of the ethyl radical to the neighboring carbon atom and the ketene which formed was hydrolyzed in an acid medium to acetic acid.



Since our results differ greatly from those obtained by Favorskii and Onishchenko with trimethyl acetylenyl ethylene glycol [2], we decided to repeat that work. The dimethylacetylenyl carbinol needed for the synthesis of this glycol was obtained by the method of Favorskii and was hydrated by the Kucherov process.

The synthesis of the glycol from the ketoalcohol was carried out in liquid ammonia. The resulting trimethyl acetylenyl ethylene glycol (IV) was treated with concentrated sulfuric acid at -10°. The reaction went in two directions: giving the same β-diketone as before [2] with a yield of about 10%, and 2,2,3-trimethyl-4-ketotetrahydrofuran (VI) with a yield of 50%.



(IV) (VI) (V)

The diketone (V) contained admixed furanone (VI) since under the action of 2,4-dinitrophenylhydrazine, besides a di-2,4-dinitrophenylhydrazone we obtained a mono-2,4-dinitrophenylhydrazone identical with that which was obtained from furanone (VI). The melting point of the disemicarbazone obtained from diketone (V) agreed with the literature data [2].

After purification from unsaturated impurities, the tetrahydrofuranone (VI) was photographed in the infrared and the spectrum confirmed the presence of the carbonyl group (1695 cm^{-1}) and the ether oxygen (1105 cm^{-1}) [4]. When the furanone was distilled with 30% potassium hydroxide it gave methyl isopropyl ketone, and acetic acid was isolated from the alkaline solution.

Thus, under the action of concentrated sulfuric acid on trimethyl acetylenyl ethylene glycol the main direction is the transformation to the substituted tetrahydrofuranone; also, to a small extent there is a pinacoline rearrangement accompanied by hydration of the triple bond.

EXPERIMENTAL

Transformations of 3,4-Dimethyl-1-Hexyn-3,4-Diol (II)

A. V. Marshueva

The starting alcohol, methyl ethyl acetylenyl carbinol, was synthesized by the Favorskii method with a yield of about 60%. Hydration of the alcohol was carried out by the Kucherov method: 4.2 g of mercuric oxide was dissolved in 25 ml of concentrated sulfuric acid and poured into 150 ml of water. We introduced dropwise with stirring into the cooled solution over a period of 2.5 hours, 49 g of methyl ethyl acetylenyl carbinol. We extracted with ether, dried, distilled off the ether, and rectified. Yield of ketoalcohol 70% and above.

B.p. 150-152°, nD^{20} 1.4215, d_4^{20} 0.9396, MR_D 31.34. $C_6H_{12}O_2$. Calculated 31.40.

Literature data [3]: b.p. 151-153°, nD^{20} 1.4215, d_4^{20} 0.9406, MR_D 31.30.

2,4-Dinitrophenylhydrazone, m.p. 164-165°.

Synthesis of the acetylenic glycol (II) from the ketoalcohol was carried out in three ways: 1) by the method of Iotsich, 2) by the method of Onishchenko, and 3) by the action of sodium acetylide in liquid ammonia. The reaction by the Iotsich method did not occur and the ketoalcohol was recovered; by the Onishchenko method the yield of glycol did not exceed 25%; by the third method the yield of glycol was much higher; the experiment was carried out under conditions given in the literature for the synthesis of acetylenic alcohols [5] which we used in the previous work [1] on the synthesis of acetylenic glycols.

3,4-Dimethyl-1-hexyn-3,4-diol (II) was obtained with a yield of 82%.

B.p. 91° (9 mm), nD^{20} 1.4670, d_4^{20} 0.9874.

Literature data [3]: b.p. 82-83.5° (7 mm), nD^{20} 1.4670, d_4^{20} 0.9901.

Reaction of glycol (II) with concentrated sulfuric acid. In a round-bottomed flask fitted with a stirrer we poured 80 ml of concentrated sulfuric acid and then with stirring and cooling to -10° we added by drops in the course of 1.5 hours 10 g of pinacone. The reaction mass was stirred for some time further, brought to room temperature, and poured onto 0.6 kg of fine ice. After salting out with ammonium sulfate, the product was extracted with ether; the ether extract was dried with sodium sulfate, the ether was distilled off, and the residue was distilled in a vacuum. As a result of the distillation we obtained two substances.

The first substance, with a yield of 14%, had b.p. 45-48° (43 mm), nD^{20} 1.4293, d_4^{20} 0.8814. The substance gave a heavy precipitate of silver acetylide, gave no reaction for hydroxyl, and formed a 2,4-dinitrophenylhydrazone with m.p. 110-110.5° (from alcohol).

Found %: C 55.59, 55.57; H 5.59, 5.73; N 18.24. $C_{14}H_{16}O_4N_4$. Calculated %: C 55.26; H 5.26; N 18.42.

On the basis of the analysis and properties of the substance, we consider it 3-methyl-3-ethyl-1-pentyn-4-one (I).

The second substance, with a yield of 40-45%, had b.p. 86-87° (42 mm). The substance was not completely pure and contained admixtures of unsaturated compounds. For purification it was oxidized with a solution of potassium permanganate; we used 3 g of $KMnO_4$ per 12 g of substance. After the usual treatment we isolated 9 g of substance which reacted neither with ammoniacal silver oxide solution nor with methyl magnesium iodide, did not decolor a solution of $KMnO_4$ and gave a precipitate of a 2,4-dinitrophenylhydrazone.

B.p. 76-77° (14 mm), nD^{20} 1.4360, d_4^{20} 0.9557, MR_D 38.85; Calc. 38.63.

Found %: C 67.68, 67.55; H 9.92, 9.98. M 141. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.86. M 142.

2,4-Dinitrophenylhydrazone of 2,3-dimethyl-2-ethyl-4-ketotetrahydrofuran (III). M.p. 122-123°.

Found %: C 52.12, 51.92; H 5.87, 5.67; N 17.84, 17.60. $C_{14}H_{18}O_5N_4$. Calculated %: C 52.17; H 5.59; N 17.39.

Reaction of 2,3-dimethyl-2-ethyl-4-ketotetrahydrofuran with a 30% solution of potassium hydroxide. A mixture of 13.7 g of furanone and 58 ml of 30% aqueous potassium hydroxide (the reaction did not go with a 20% solution) was distilled from a Wurtz flask. The concentration of the solution was kept constant by addition of water from a dropping funnel. The resulting distillate was saturated with ammonium chloride, extracted with ether, and dried with sodium sulfate. After removal of the ether and distillation at atmospheric pressure we obtained 4.5 g of substance.

B.p. 118-120°, nD^{20} 1.4000, d_4^{20} 0.8219, MR_D 29.94, $C_6H_{18}O$. Calculated 29.92.

Literature data for methyl sec-butyl ketone [6]: b.p. 118°, nD^{20} 1.4002, d_4^{18} 0.8181; for ethyl isopropyl ketone [7]: b.p. 118-120°, nD^{20} 1.4020, d_4^{20} 0.8014.

The substance gives a semicarbazone with m.p. 217-218° and a 2,4-dinitrophenylhydrazone with m.p. 71-72° (from alcohol).

Found %: C 51.30; 51.61; H 5.80; 5.89; N 20.37; 20.07. $C_{12}H_{16}O_4N_4$. Calculated %: C 51.43; H 5.71; N 20.00.

The alkaline solution after distillation of the neutral product was acidified with sulfuric acid and we distilled off acetic acid with steam. The silver salt was analyzed.

Found %: Ag 64.61, 64.63. $C_2H_3O_2Ag$. Calculated %: 64.67.

These results show that as a result of alkaline hydrolysis we obtained methyl sec-butylketone and acetic acid.

Transformations of 3,4-Dimethyl-1-Pentyn-3,4-Diol (IV)

Hsu Ting-yu

The starting dimethylacetylenyl carbinol was obtained by the Favorskii method; its constants agreed with the literature data. Hydration of this alcohol according to Kucherov gave dimethylacetyl carbinol with b.p. 139-140° [2].

Synthesis of trimethyl acetylenyl ethylene gylcol (IV) was carried out under the conditions described for the synthesis of acetylenic alcohols by the method described in the literature [5] in liquid ammonia. Yield 53%.

B.p. 81-83° (9 mm), nD^{20} 1.4603, d_4^{20} 0.9991, MR_D 35.05. $C_7H_{12}O_2F$. Calculated 35.56.

Literature data [2]: b.p. 86-88° (14 mm), nD^{20} 1.4638, d_4^{20} 1.0032.

Reaction of trimethyl acetylenyl ethylene glycol with sulfuric acid. The reaction was carried out under the conditions described above for 3,4-dimethyl-1-hexyn-3,4-diol. The resulting product was vacuum distilled. We obtained two fractions.

First fraction b.p. 64-68° (15 mm), 2 g, nD^{20} 1.4295; second fraction b.p. 68-69.5° (15 mm), 8 g, nD^{20} 1.4330, d_4^{20} 0.9586, MR_D 34.69. $C_7H_{12}O_2$. Calculated 34.55 (both oxygens carbonyl).

Literature data [2]: b.p. 57-58.5° (10 mm), 173-174°, nD^{20} 1.4306, d_4^{20} 0.9575.

Found %: C 44.57; 44.74; H 7.75; 7.63; N 34.65. $C_9H_{18}O_2N_6$. Calculated %: C 44.62; H 7.40; N 34.71.

The product obtained by the action of 2,4-dinitrophenylhydrazine after recrystallization from alcohol was separated into two substances: a yellow one with m.p. 210°, and a red one with m.p. 143°.

Found for the yellow substance %: N 22.98, 23.20. $C_{19}H_{18}O_8N_8$. Calculated %: N 23.04.

The substance was a di-2,4-dinitrophenylhydrazone.

Found for the red substance %: N 18.29, 18.57. $C_{13}H_{16}O_4N_4$. Calculated %: N 18.20.

These results correspond to a mono-2,4-dinitrophenylhydrazone.

Since the substance of the second fraction, with b.p. 68-69.5° (15 mm), decolorized a solution of potassium permanganate, it was oxidized by this solution. In the oxidation of 3.3 g of the substance we used 100 ml of a 1% solution of $KMnO_4$. After the usual treatment we obtained 2 g of a neutral substance.

B.p. 170° n_D^{20} 1.4260, d_4^{20} 0.9494, MR_D 34.54. $C_7H_{12}O_2$. Calculated 34.55 (both oxygens carbonyl), 33.98 (one carbonyl oxygen, one ether).

The resulting product no longer decolorized $KMnO_4$ nor gave a semicarbazone; under the action of 2,4-dinitrophenylhydrazine it gave a mono-2,4-dinitrophenylhydrazone with m.p. 143-144°. A sample mixed with the 2,4-dinitrophenylhydrazone obtained previously gave no melting point depression. Hydroxyl groups were absent in this compound.

The product obtained after oxidation was thus 2,2,3-trimethyl-4-ketotetrahydrofuran (VI); its structure was confirmed by a photograph of the infrared spectrum.

Reaction of 2,2,3-trimethyl-4-ketotetrahydrofuran with an aqueous solution of potassium hydroxide. Two g of the substance were distilled in a Wurtz flask with 25 ml of 20% potassium hydroxide solution. The concentration of the solution was maintained by continuous dripping in of water. The resulting distillate was treated with 2,4-dinitrophenylhydrazine; we obtained a 2,4-dinitrophenylhydrazone with m.p. 115-116°. The 2,4-dinitrophenylhydrazone of methyl isopropyl ketone melts at 117° [8].

Found %: N 21.10, 21.12. $C_{11}H_{14}O_4N_4$. Calculated %: N 21.04.

The alkaline solution which remained after distillation of the methyl isopropyl ketone was concentrated on a water bath, acidified with sulfuric acid, and extracted with ether. The residue after removal of the ether was converted to the silver salt.

Found %: Ag 64.45, 64.85. $C_2H_3O_2Ag$. Calculated %: Ag 64.67.

SUMMARY

1. We have showed that ditertiary α-glycols with free acetylenic hydrogen, 3,4-dimethyl-1-hexyn-3,4-diol and trimethyl acetylenyl ethylene glycol, are transformed under the action of concentrated sulfuric acid at -10° into derivatives of 4-ketotetrahydrofurans, which are the chief products of the reaction.

2. A secondary direction of the reaction is a pinacoline rearrangement, as a result of which in the first case is formed the acetylenic ketone, 3-methyl-3-ethyl-1-pentyn-4-one; in the second case the product is formed by hydration of the acetylenic ketone, a β-diketone, dimethyl acetyl acetone.

3. Both 4-ketotetrahydrofurans are split when heated with aqueous solutions of alkali into ketene, which is further hydrolyzed into acetic acid, and methyl sec-butyl ketone in the first case, and methyl isopropyl ketone in the second.

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POLYENE COMPOUNDS

XII.* THE CONDENSATION OF 5-PHENYL-2,3-PENTADIENAL WITH ARYLACETIC ACIDS

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It was shown in previous work [1] that on the basis of 5-phenyl-2,4-pentadienal it was easy to obtain unsymmetrical 1,6-diaryl-substituted 1,3,5-hexatrienes which have luminescent properties. In developing these studies we have made a more detailed investigation of the reaction between 5-phenyl-2,4-tetradienal and substituted aryl acetic acids in order to obtain new examples of unsymmetrical 1,6-diarylhexatrienes.

The reaction between 5-phenyl-2,4-pentadienal and 2,4-dimethyl-, 3,5-dimethyl-, 2,4,5-trimethyl-, p-methoxy-, p-nitrophenylacetic, 2-methyl- and 4-methylnaphthyl-1-acetic acids was carried out under conditions described by Kuhn [2] in the presence of acetic anhydride and lead oxide. As a result of the reaction we obtained 1-phenyl-6-aryl derivatives of 1,3,5-hexatriene by the scheme

$$C_6H_5CH{=}CH{-}CH{=}CH{=}CHO + RCH_2COOH \rightarrow C_6H_5(CH{=}CH)_3R + H_2O + CO_2$$

(I) R = 2,4-$(CH_3)_2C_6H_3$, (II) R = 3,5-$(CH_3)_2C_6H_3$, (III) R = p-$CH_3OC_6H_4$, (IV) R = p-$NO_2C_6H_4$, (V) R = 4-$CH_3C_{10}H_6$.

It follows from these experiments that the yield of hexatriene derivatives depends on the position of the substitutent in the benzene ring of the arylacetic acid. This is especially clear in the example of the methyl-substituted acids. We showed that in the reaction of 3,5-dimethylphenylacetic acid with 5-phenyl-2,4-pentadienal we obtained about the same yield (39%) of hexatriene derivative as in the case of reaction of this aldehyde with unsubstituted phenylacetic acid from which, as we showed earlier [1] 1,6-diphenyl-1,3,5-hexatriene was formed with a yield of 34.5%. Thus, the introduction of a methyl group in the meta position of phenylacetic acid had little effect on the reactivity of the methylene groups. On the contrary, in the presence in phenylacetic acid of one methyl group in the ortho position, the reaction with 5-phenyl-2,4-pentadienal was much more difficult, and with two ortho-methyl groups it did not occur at all. Thus, 2,4-dimethylphenylacetic acid in the reaction with 5-phenyl-2,4-pentadienal gave only a 10% yield of 1-phenyl-6-(2,4-dimethylphenyl)-1,3,5-hexadiene, and 2,4,6-trimethylphenylacetic acid did not react at all with this aldehyde.

The same difference occurred with respect to 5-phenyl-2,4-pentadienal and methylnaphthylacetic acids. While 4-methylnaphthyl-1-acetic acid gave almost the same yield of hexatriene compound as unsubstituted naphthylacetic acid [1], 2-methylnaphthyl-1-acetic acid under the same conditions did not react with 5-phenyl-2,4-pentadienal. In the case of 2,4,6-trimethylphenylacetic acid and 2-methylnaphthyl-1-acetic acid under the conditions described above we isolated only the lead salt of these acids (VI, VII), and did not obtain a hexatriene compound.

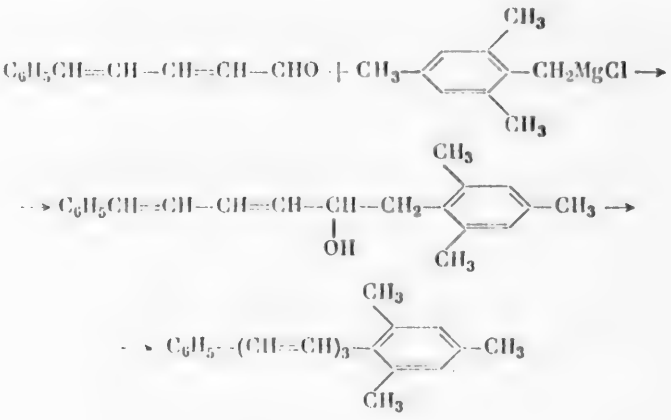
* Communication XI, cf. Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk, 1267 (1960).

1-Phenyl-6-Aryl-1,3,5-Hexatrienes $C_6H_5(CH=CH)_3R$

Compound No.	R	Yield, %	M.p.	Solvent	Found, %			Calculated, %		
					C	H	N	C	H	N
(I)	$2,4\text{-}(CH_3)_2C_6H_3$	10.2	107—108°	Alcohol	91.85	7.96	—	92.26	7.74	—
(II)	$3,5\text{-}(CH_3)_2C_6H_3$	39.0	129—129.5	Alcohol	92.15	7.91	—	92.26	7.74	—
(III)	$p\text{-}CH_3OC_6H_4$	22.1	185.5—187	Benzene	86.88	6.95	—	86.99	6.91	—
(IV)	$p\text{-}NO_2C_6H_4$	30.5	194—196	Dioxane	78.06	5.72	5.04	77.93	5.49	5.05
(V)	$4\text{-}CH_3C_{10}H_6$	19.2	169—170	Benzene	93.26	6.76	—	93.20	6.80	—

The inertness of the methylene groups of 2,4-dimethylphenylacetic acid and especially of 2,4,6-trimethylphenylacetic acid and 2-methylnaphthyl-1-acetic acid is evidently connected with special difficulties.

Since we did not succeed in obtaining 1-phenyl-6-(2,4,6-trimethylphenyl)-1,3,5-hexatriene from 2,4,6-trimethylphenylacetic acid, we used for the preparation of this compound (which is interesting because of its luminescent properties) the reaction between 5-phenyl-2,4-pentadienal and 2,4,6-trimethylbenzyl magnesium chloride. As a result of this reaction we isolated 1-phenyl-5-hydroxy-6-(2,4,6-trimethylphenyl)-1,3-hexadiene (VIII), which by dehydration with hydrobromic acid was converted into 1-phenyl-6-(2,4,6-trimethylphenyl)-1,3,5-hexatriene (IX).



EXPERIMENTAL

1-Phenyl-6-aryl-1,3,5-hexatrienes. A mixture of 0.01 mole of substituted arylacetic acid, 0.01 mole of 5-phenyl-2,4-pentadienal, 2 ml of acetic anhydride, and 1.2 g of litharge was boiled under reflux for five hours in a nitrogen atmosphere. After cooling to room temperature, the reaction mass crystallized. The precipitate was filtered off, washed with a mixture of benzene or acetone with alcohol, chromatographed on aluminum oxide, and recrystallized. The results are given in the table.

Lead salt of 2,4,6-trimethylphenylacetic acid (VI). A mixture of 2.55 g of 5-phenyl-2,4-pentadienal, 5 ml of acetic anhydride, and 4.4 g of litharge was boiled under reflux for five hours in a stream of nitrogen. On the next day the crystallized mass was treated with 10 ml of alcohol and the precipitate was filtered off (4.22 g, m.p. 148-205°). After crystallization from benzene we obtained 3.4 g of substance with m.p. 208-215°, which after several crystallizations from xylene had m.p. 232-234° and, from the analytical results, was lead 2,4,6-trimethylphenylacetate.

Found %: C 46.40, 46.25; H 4.71, 4.42; ash 39.93, 39.99. $C_{22}H_{26}O_4Pb$. Calculated %: C 47.04; H 4.67; ash 39.75.

Lead salt of 2-methylnaphthyl-1-acetic acid (VII). A mixture of 3.2 g of 2-methylnaphthyl-1-acetic acid,

2.52 g of 5-phenyl-2,4-pentadienal, 2 ml of acetic anhydride, and 1.2 g litharge was boiled for five hours in a stream of nitrogen. After addition to the mixture of 10 ml of an equal amount of benzene and alcohol, we obtained 0.65 g (20%) of the lead salt of 2-methylnaphthyl-1-acetic acid, which after several crystallizations from dioxane appeared as fine colorless plates with m.p. 234-236°.

Found %: C 51.54; 51.36; H 3.71; 3.65; ash 36.88, 36.79. $C_{26}H_{22}O_4Pb$. Calculated %: C 51.56; H 3.67; ash 36.87.

From the mother liquor we could not isolate 1-phenyl-6-(2-methylnaphthyl-1)-1,3,5-hexatriene.

1-Phenyl-5-hydroxy-6-(2,4,6-trimethylphenyl)-1,3-hexadiene (VIII). To a mixture of 18.8 g of magnesium and 170 ml of absolute ether cooled with ice water we added in the course of 2.5 hours a solution of 13 g of 2,4,6-trimethylbenzyl chloride in 400 ml of absolute ether. The reaction mass was kept for two hours with ice cooling, then heated to room temperature and the excess magnesium was filtered off. To the resulting Grignard reagent we added over the period of an hour and with vigorous stirring a solution of 7.6 g of 5-phenyl-2,4-pentadienal in 150 ml of absolute ether. On the next day the reaction mixture was decomposed with 40% acetic acid, the ether solution was separated, washed several times with water, and dried over potash. After distillation of the ether we obtained 19.7 g of a light-yellow, viscous oil. When we fractionated 8.5 g of this oil in a vacuum, we separated two main fractions which crystallized on cooling. From the first fraction with b.p. 140-150° (6 mm) (1.9 g) after crystallization from alcohol we obtained dimesitylethane with m.p. 117-118°, which agreed with the literature data [3]. From the second fraction with b.p. 150-175° (6 mm) (2.8 g) after crystallization from acetone and then two crystallizations from alcohol, we obtained 1-phenyl-5-hydroxy-6-(2,4,6-trimethyl)-1,3-hexadiene with m.p. 107-109°.

Found %: C 85.68, 85.67; H 8.07, 8.16. $C_{21}H_{24}O$. Calculated %: C 86.26; H 8.27.

1-Phenyl-6-(2,4,6-trimethylphenyl)-1,3,5-hexatriene (IX). A solution of 3 g of the oily product from the 19.7 g obtained in the previous experiment was boiled in 10 ml of acetone for 10 minutes with 0.4 ml of concentrated hydrobromic acid. After cooling the mixture to room temperature, the resulting precipitate was filtered off and washed with acetone. We obtained 0.47 g (22%) of 1-phenyl-6-(2,4,6-trimethylphenyl)-1,3,5-hexatriene with m.p. 129-131°. After chromatography on aluminum oxide (solvent hexane) and subsequent crystallization from acetone, 1-phenyl-6-(2,4,6-trimethylphenyl)-1,3,5-hexadiene appeared as colorless crystals with m.p. 131.5-132.5° and with a bright luminescence in the solid state and in benzene solution when illuminated with ultraviolet light.

Found %: C 91.60, 91.65; H 8.08, 8.13. $C_{21}H_{22}$. Calculated %: C 91.92; H 8.08.

SUMMARY

1. We have studied the reaction between 5-phenyl-2,4-pentadienal and arylacetic acids. In this way we have obtained a series of 1-phenyl-6-aryl derivatives of 1,3,5-hexatriene with luminescent properties.

2. We have established that the presence of a methyl group in the ortho position to the methylene group of the arylacetic acid hinders the formation of hexatriene derivatives.

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STUDIES IN THE FIELD OF THE CHEMISTRY OF ORGANIC OXIDES

XVIII. THE ORDER OF ADDITION OF ALCOHOLS TO CHLOROPRENE OXIDE IN THE PRESENCE OF ALCOHOLATES AND BORON FLUORIDE ETHERATE

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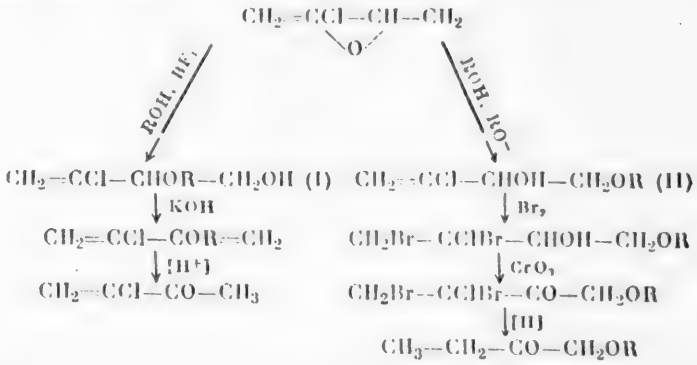
In the previous work one of us showed that alcohols add to divinyl oxide in the presence of alcoholates, preferably with formation of secondary alcohols, and in the presence of boron fluoride etherate, and acids, with the formation of primary alcohols [1]. The conclusion was confirmed in the following years by a series of chemists [2, 3]. The addition of alcohols to isoprene oxide [4] and piperylene oxide [5] also proceeds according to this rule. Thus, for example, in the reaction of isoprene oxide with methanol and ethanol in the presence of alcoholates we obtained altogether about 10% of the primary alcohol, and in the presence of boron fluoride etherate, only the primary alcohol was obtained [4].

We set out to establish the order of addition of alcohols to chloroprene oxide (3-chloro-1,2-epoxy-3-butene). Of the addition reactions of this oxide only hydration, addition of hydrogen halides, and catalytic hydrogenation have been studied.•

By hydration of chloroprene oxide was obtained 3-chloro-3-buten-1,2-diol [6]. The addition of hydrogen halides occurred preferably with formation of a primary alcohol [6]. In hydrogenation over $Pd/CaCO_3$ the oxide ring was also broken on the side of the secondary carbon atom, and there occurred partial addition of hydrogen in the 1,4-position [7].

Our experiments showed that methyl and ethyl alcohols add to chloroprene oxide in the presence of boron fluoride etherate with formation of the primary alcohol (I).



• At the time this paper went to press, the work of E. G. Hawkins was not known to us [13].

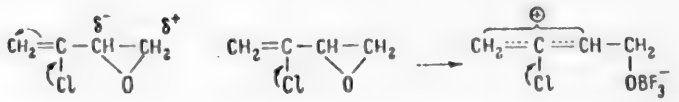
This was shown chiefly by the phthalate method. Also, alcohol (I) was dehydrated over KOH to the previously described chloroalkoxyprene which was then converted by the action of dilute sulfuric acid to methyl chlorovinyl ketone (identified as the 2,4-dinitrophenylhydrazone).

The addition of methyl and ethyl alcohols to chloroprene oxide in the presence of alcoholates occurs preferably with formation of the secondary alcohol (II). The phthalate method showed about 30% of the primary alcohol in the resulting product.

The structure of the chief products was shown by their conversion by bromination, oxidation, and then reduction to the alkoxyacetones which in turn were identified by the melting points of their 2,4-dinitrophenylhydrazones.

To show the presence in the adducts of admixtures of primary alcohols, besides the phthalate reaction, we used the conversion to the chloroalkoxyprenes by distillation in a vacuum over KOH. Here the secondary alcohols were not changed. The yield of chloroalkoxyprenes was small, but their presence was undoubted.

Thus, as a result of the study, we have established that chloroprene oxide adds alcohols in a different order depending on the nature of the catalyst. As compared to divinyl oxide it gives more primary alcohol in the reaction with alcoholates. If we start from the previous ideas of the mechanism of addition of alcohols to organic oxides in the presence of alkaline and acid catalysts, then these experimental facts mean that under the influence of a chlorine atom the positive inductive effect of the vinyl radical is weakened, and hence the difference in polarization of carbon atoms C_1 and C_2 is lessened, which in turn lessens the selectivity in the rupture of the oxide



ring at the moment of nucleophilic attack. In the reaction of chloroprene oxide with alcohols in the presence of boron fluoride, the chlorine atom cannot shift the rupture of the oxide ring toward C_2 since only in such a rupture of the oxide bond does stabilization occur due to a conjugated intermediate complex.

It should be noted that the order of addition of alcohols to an unsaturated halogen-substituted oxide differs from the order of their addition to a saturated oxide of the same type. In the latter case the nature of the catalyst tells considerably less about the order of addition, and there is always preference for the secondary alcohols [8]. Such behavior of the saturated substituted oxides is explained by the vicinal effect [9, 10]. In the case of halogen-substituted vinyl oxides there is first decreased the polarization of the C-Hal bond, and second, a marked role is played by the above-mentioned stabilization of the conjugated intermediate complex.

EXPERIMENTAL

Chloroprene oxide was obtained from chloroprene through the bromohydrin by the method described previously [6].

Addition of alcohols in the presence of boron fluoride etherate. a) Addition of methyl alcohol. To a solution of 10 g of chloroprene oxide in a ten fold excess of methyl alcohol with cooling to 0 to -3° we added 0.2 ml of boron fluoride etherate. The reaction mixture was stirred for two hours with cooling and then for three hours at room temperature, after which the boron fluoride was decomposed by addition of 0.4 ml of 0.5 N KOH. The alcohol was distilled off at ordinary pressure and the reaction product was distilled in a vacuum. The yield of 2-methoxy-3-chloro-3-buten-1-ol was 8 g (61.5%).

B.p. 82-83° (20 mm), d_4^{20} 1.1479, nD^{20} 1.4610, MR 32.65; Calc. 32.89.

Found %: C 43.84; H 6.78; Cl 25.58, 25.97; primary alcohol (phthalation) [11] 99.5. $C_5H_9O_2Cl$. Calculated %: C 43.96; H 6.64; Cl 26.96.

We slowly distilled 5.1 g of the substance over 8.5 g of powdered KOH so that the temperature of the vapor did not rise above 104°. The upper layer of distillate was separated from the water, dried with potash, and distilled

in a vacuum. We obtained about 1.3 g of chloromethoxyprene with b.p. 55-60° (40 mm) [12]. The substance dissolved in the cold in 2% H_2SO_4, being converted to methyl chlorovinyl ketone, whose 2,4-dinitrophenylhydrazone had a m.p. 153-154° (from alcohol).

Found %: N 20.04. $C_{10}H_9O_4N_4Cl$. Calculated %: N 19.67.

b) Addition of ethyl alcohol. From 10 g of chloroprene oxide under the conditions described above we obtained 8 g (55.5%) of 2-ethoxy-3-chloro-3-buten-1-ol.

B.p. 87-88° (20 mm), d_4^{20} 1.0960, nD^{20} 1.4575, MR 37.46; Calc. 37.48.

Found %: C 47.92; H 7.33; Cl 23.19; primary alcohol 99.1. $C_6H_{11}O_2Cl$. Calculated %: C 47.85; H 7.36; Cl 23.54.

Dehydration of 4.3 g of the substance under the above conditions gave 1.2 g of ethoxychloroprene, which was then converted into methyl chlorovinyl ketone. The 2,4-dinitrophenylhydrazone, m.p. 153-154° (from alcohol).

Addition of alcohols in the presence of alcoholates. a) Addition of methyl alcohol. A solution of 10 g of chloroprene oxide in methyl alcohol (twenty fold excess) in which had first been dissolved 0.5 g of metallic sodium was heated for six hours under reflux on a water bath, after which the excess methyl alcohol was distilled with a rectifying column and the residue distilled in a vacuum. We thus obtained 6 g (47% on the oxide) of a mixture of 1-methoxy-3-chloro-3-buten-2-ol and 2-methoxy-3-chloro-3-buten-1-ol.

B.p. 77-78° (20 mm), d_4^{20} 1.1323, nD^{20} 1.4595, MR 33.00; Calc. 32.89.

Found %: C 43.86; H 6.77; Cl 25.57; primary alcohol 30.5, 31.8. $C_5H_9O_2Cl$. Calculated %: C 43.96; H 6.64; Cl 25.96.

We dissolved 5.6 g of the substance in 20 ml of chloroform and brominated it with cooling (0°) and stirring of the chloroform solution of 7 g of bromine. We obtained 8.5 g of dibromide.

B.p. 124° (5 mm), d_4^{20} 1.8570, nD^{20} 1.5343, MR 49.80; Calc. 49.95.

Found %: Cl + 2Br 65.66, 65.61. $C_5H_9OClBr_2$. Calculated %: Cl + 2Br 65.65.

The dibromide was dissolved in acetic acid and the resulting solution was treated with the calculated amount of potassium bichromate and then at 20° (external cooling) and good stirring we added dropwise 25% H_2SO_4 (the calculated amount). After the mixture was neutralized, the ketone was extracted with ether in a mechanical extracter, the ether was distilled off, and the residue without distillation was reduced with 2% sodium amalgam (400 g) in acetic acid.

From the resulting solution we isolated about 1.5 g of methoxymethylethyl ketone with b.p. 128-135°. The 2,4-dinitrophenylhydrazone had m.p. 197.5° (from ethyl acetate) which agrees with the literature data [1].

b) Addition of ethyl alcohol. From 10 g of oxide we obtained 9.5 g (60%) of a mixture of 1-ethoxy-3-chloro-3-buten-2-ol and 2-ethoxy-3-chloro-3-buten-1-ol.

B.p. 84.5-85.5° (20 mm), d_4^{20} 1.0914, nD^{20} 1.4568, MR 37.57; Calc. 37.48.

Found %: C 48.08; H 7.32; Cl 23.16; primary alcohol 37.1, 35.7. $C_6H_{11}O_2Cl$. Calculated %: C 47.85; H 7.36; Cl 23.54.

Bromination of the substance, oxidation of the bromohydrin, and reduction of the resulting ketone gave ethoxymethylethyl ketone. The 2,4-dinitrophenylhydrazone had m.p. 145-146° (from ethyl acetate) which agreed with the literature data [1].

SUMMARY

1. We have studied the order of addition of methyl and ethyl alcohols to chloroprene oxide in the presence of boron fluoride etherate and alcoholates.

2. We have established that in the presence of boron fluoride there occurs formation of a primary alcohol, and in the presence of alcoholates, of a secondary alcohol with an admixture of about 35% of the primary alcohol.

3. We have suggested a mechanismfor the influence of the chlorine atom on the order of rupture of the oxide ring in alkaline and acid catalysis.

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STUDIES IN THE FIELD OF CONJUGATED SYSTEMS

CXXIII. CHLOROARYLATION OF VINYLETHYLACETYLENE*

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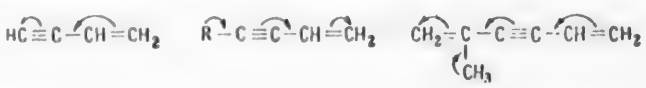
In recent years in our laboratory we have studied some of the main regularities in the reactivities of different types of structures of vinylacetylene hydrocarbons in relation to electrophilic, nucleophilic, and radical reagents and have studied especially the reaction of vinylacetylenes with lithium alkyls [1], lithium amides [2], and diazonium salts [3]. We have shown that these reactions usually occur at the ethylenic bond with formation of acetylene (3,4-derivatives) or allene (1,4-derivatives). Thus, for example, in the chloroarylation of vinylacetylene there is obtained a mixture of 2-chloroaryl-3-butyne and, apparently, 4-chloroaryl-2,3-butadiene [3].

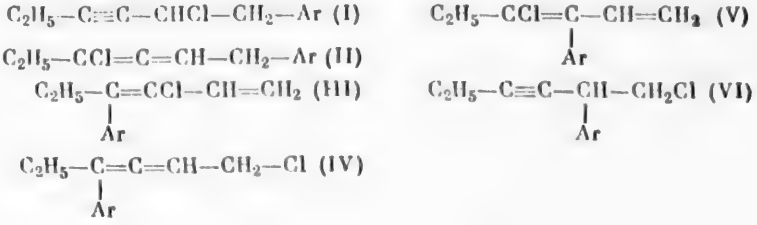
The reaction of chloroarylation of vinyl and isopropenylacetylene was studied in detail previously by A. V. Dombrovskii [4] but the formation of allenic compounds was not noted by him.

Chloroarylation of vinylalkylacetylenes has not yet been studied. Also, the reaction of vinylalkylacetylenes with diazonium salts is of considerable interest since in these compounds there are differently polarized conjugated systems under the influence of radicals than in unsubstituted vinylacetylene.



Our studies were of the chloroarylation of vinylethylacetylene by the action of phenyl-, p-tolyl-, p-chlorophenyl-, and p-anisyldiazonium chlorides. In all cases we obtained substances with the formula $Ar\text{-}C_6H_8Cl$.

As a result of the reaction with diazonium salts we can here expect the formation of six different products:



The choice between all the possible formulas for the substance actually obtained in the reaction of vinylethylacetylene with phenyl diazonium chloride was made by us on the basis of a study of their catalytic hydrogenation, ozonization, and infrared spectra.

*Enyne compounds. XLIV

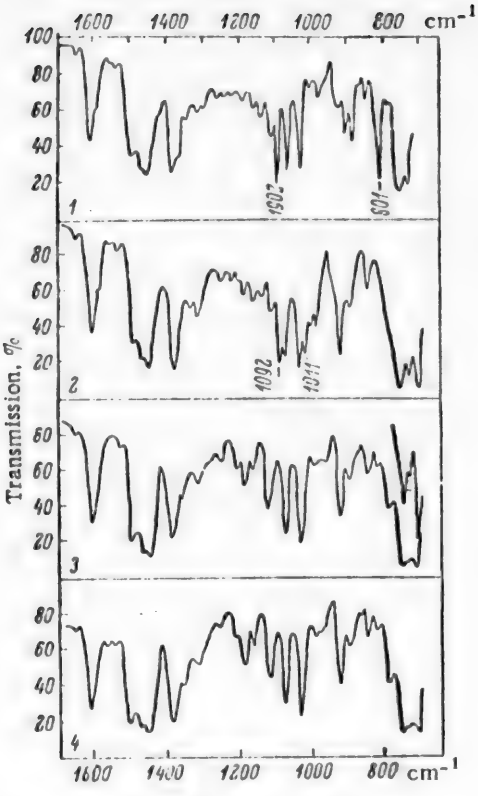


Fig. 1. Infrared transmission spectra (100 μ). 1) 3-Phenylhexane; 2) 2-phenylhexane; 3) 1-phenylhexane; 4) product of hydrogenation of 2-chloro-1-phenyl-3-hexyne with an admixture of allene isomer.

a) As a result of hydrogenation of phenyl-chlorohexyne and hexadiene (I)-(VI) we can expect formation of three phenylhexanes: 1-phenylhexane from (I) and (II), 2-phenylhexane from (VI), and 3-phenylhexane from (III), (IV), and (V). All these phenylhexanes are described in the literature and differ greatly in boiling point and infrared spectra (Fig. 1).

In the infrared spectra of the isomers with branched chains there is an intense band at 1092 cm^{-1} which is absent in the spectrum of 1-phenylhexane. 2-Phenylhexane differs from its isomers by an intense absorption in the region 1011 cm^{-1}, and 3-phenylhexane has the same intense absorption in the region of 801 cm^{-1}. There are other differences in the intensity of bands in the region 880-920 cm^{-1}.

The boiling point and infrared spectrum of the phenylhexane obtained as a result of hydrogenation of the product of chloroarylation of vinylethylacetylene agreed with the data for 1-phenylhexane. The low frequencies in the region 801, 1011, and 1092 cm^{-1} do not occur in this spectrum. Thus it was established that chlorophenylation of vinylethylacetylene goes with formation of substances with only the normal structure, and so formulas (III)-(VI) are excluded.

b) In the infrared spectrum of the product of chlorophenylation of vinylethylacetylene there is a rather intense absorption in the region of 2220 cm^{-1} and a weak absorption at 1970 cm^{-1}.

Hence this is 2-chloro-1-phenyl-3-hexyne (I) with a slight admixture of the allenic isomer (II) (Fig. 2, curve 2).

These conclusions as to the structure of products of chlorophenylation of vinylethylacetylene can be extended also to other products of chloroarylation, since their infrared spectra are of the same type. For instance, in all the spectra we find the same ratio in intensity of bands at 2220 and 1970 cm^{-1}, the absence of an intense band in the region above 3050 cm^{-1} and in the region of 970-1000 cm^{-1}, which could indicate the presence of the third possible isomer with conjugated double bonds. The intensity of the frequency of valence oscillation of the double bonds (benzene ring) is small in all the spectra except the spectrum of chloroanisylhexyne; the high intensity of this frequency is characteristic for the spectrum of unsubstituted anisole also (Fig. 2, curves 3-5).

c) As a result of ozonization of the chlorophenylation products we obtained propionic and evidently α-chlorohydrocinnamic acid, that is, substances which correspond to formula (I). Ketones which could be given by isomers (III), (IV), and (V) were not found. Phenylacetic acid was also not isolated, so that isomer (II) was evidently present in small amount.

Thus, as a result of this study it was established that the reaction of chloroarylation of vinylacetylenes occurs at a position on the double bond independent of the distribution of electron density in their molecules. The position taken by the aryl radical is always the end carbon atom of this conjugated system. In distinction from vinylacetylene, vinylethylacetylene preferably forms acetylene isomer (I); hence the presence of a radical on the triple bond increases the activity of the double bond under the influence of the previously mentioned electron shift.

In the light of these results it is interesting to determine the direction of chloroarylation of vinylisopropenylacetylene, which has two double bonds with different relationships conjugated with the triple bond.

Electrophilic addition of alkyl hypobromites to vinylisopropenylacetylene occurs on the isopropenyl group [5], radical addition of lithium alkyls is preferably on the vinyl group [6], and finally, nucleophilic addition of alcohols and water is on the acetylene bond [7].

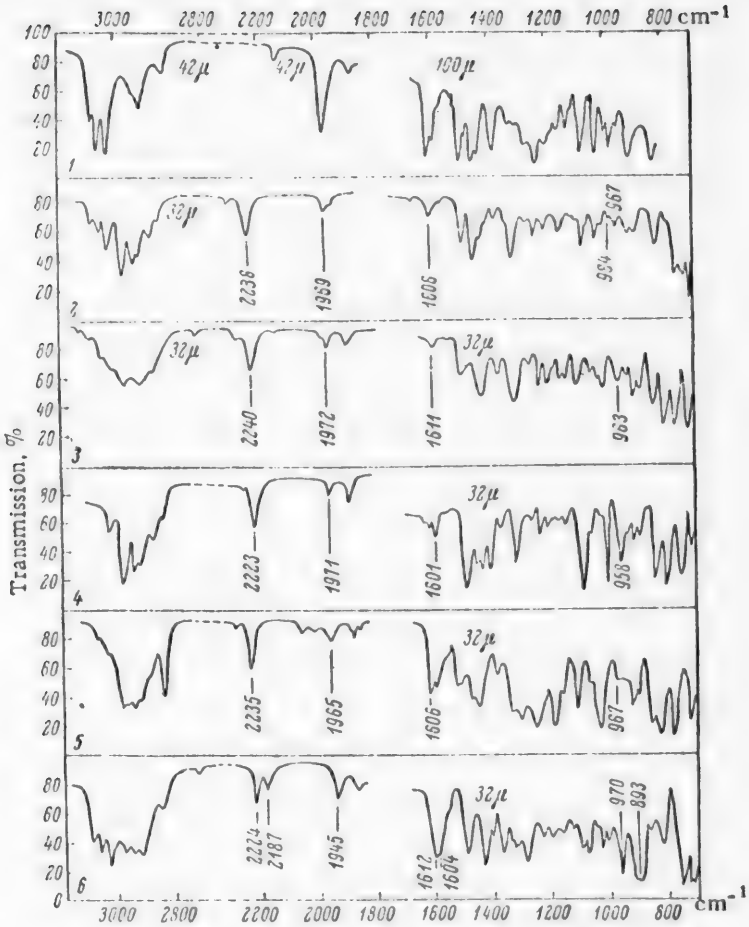


Fig. 2. Infrared spectra of chloroarylation products. 1) Vinylacetylene with phenyldiazonium chloride, 2) vinylethylacetylene with phenyldiazonium chloride, 3) vinylethylacetylene with p-tolyldiazonium chloride, 4) vinylethylacetylene with p-chlorophenyldiazonium chloride, 5) vinylethylacetylene with p-anisyldiazonium chloride, 6) vinylisopropenylacetylene with phenyldiazonium chloride.

Conclusionson the structure of the products of chlorophenylation of vinylisopropenylacetylene were made by us on the basis of comparison of their infrared spectra with the spectrum of the starting hydrocarbon. In the spectrum of the hydrocarbon there were characteristic frequencies for the vinyl group (920 and 980 cm^{-1}) and for the isopropenyl group (890 cm^{-1}) [5]. In the spectra of the products of chloroarylation there remained a very intense frequency for the isopropenyl group, and there was a marked decrease in intensity of the frequency at 900-1000 cm^{-1}, which could be assigned to the vinyl group.

Thus it was established that chloroarylation of vinylisopropenylacetylene occurs preferably on the vinyl group, that is, in the same way as was shown for the other reactions of addition of radicals. Evidently the chief role here is played by special hindrance; the methyl radical screens the double bond.

We should also note that in the case of vinylisopropenylacetylene there is formed more of the allene isomer than in the case of vinylethylacetylene. This is explained by the contrary results of the effect of an isopropenyl group on the conjugated vinylacetylene system as compared to the ethyl radical.

EXPERIMENTAL

Chloroarylation of vinylethylacetylene. Vinylethylacetylene was obtained from sodium vinylacetylide and ethyl bromide in liquid ammonia [8]; vinylisopropenylacetylene resulted from dehydration of dimethylvinylacetylenyl carbinol [9].

The method of chloroarylation did not differ from that worked out by A. V. Dombrovskii [4].

The yield, constants, and analytical results for all the products of chloroarylation are given in the table.

Substance (chief isomer)	Empirical formula	B.p. (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Found (%) C	Found (%) H	Found (%) Cl	Calculated (%) C	Calculated (%) H	Calculated (%) Cl	Yield, %
$C_6H_5-C\equiv C-CHCl-CH_3-C_6H_5$	$C_{12}H_{13}Cl$	103—104° (3)	1.0430	1.5410	58.05	56.87	74.97, 75.15	7.01, 7.09	18.62, 18.41	74.82	6.78	18.43	42
$C_6H_5-C\equiv C-CHCl-CH_2-C_6H_4-CH_3-p$	$C_{13}H_{15}Cl$	112 (2)	1.0193	1.5361	63.24	61.50	76.03, 76.11	7.57, 7.48	16.51, 17.12	75.51	7.26	17.14	54
$C_6H_5-C\equiv C-CHCl-CH_2-C_6H_4-Cl-p$	$C_{12}H_{12}Cl_2$	124—125 (2)	1.1085	1.5642	66.72	61.74	64.48	5.66		63.62	5.32		30
$C_6H_5-C\equiv C-CHCl-CH_2-C_6H_4-OCH_3-p$	$C_{13}H_{15}OCl$	123—124 (~1)	1.0767	1.5470	65.59	63.14	64.75, 65.94, 70.34	5.71, 7.01, 7.03	15.68, 15.42	70.16	6.79	15.91	32.5

Hydrogenation of 2-chloro-1-phenyl-3-hexyne. Hydrogenation of 9.4 g of the substance was carried out in 75 ml of methyl alcohol in the presence of 15 g of Pd/$CaCO_3$ for 4.5 hours. There was absorption of 3235 ml of H_2 (762.4 mm, 23°), which corresponded to 89.1%.

The reaction product was distilled with steam, salted out of the distillate by a saturated solution of $CaCl_2$, dried, and vacuum distilled. We obtained 6.4 g of hydrocarbon with an admixture of chloride. By fractionation from this mixture we obtained about 4 g of 1-phenylhexane. B.p. 109-110° (20 mm), d_4^{20} 0.8583, nD^{20} 1.4872.

Another synthesis of 1-phenylhexane was carried out in the following way. From cinnamaldehyde and propyl bromide by the magnesium organic method we obtained 1-phenyl-1-hexen-3-ol. By the action of phosphorus trichloride the alcohol was converted to the chloride. We hydrogenated 8.6 g of 3-chloro-1-phenyl-1-hexene over Pd/$CaCO_3$ (11 g) until 2615 ml of H_2 had been absorbed (758.5 mm, 22.5°), which corresponded to 96.4%. We isolated from the reaction mixture by the method of the previous experiments 6.8 g of 1-phenylhexane. B.p. 109-110° (20 mm), d_4^{20} 0.8578, nD^{20} 1.4872.

According to constants and infrared spectrum, this sample did not differ from that obtained by hydrogenation of the product of chlorophenylation of vinylethylacetylene (Fig. 1, curves 3 and 4).

The isomeric 2-phenylhexane was obtained by hydrogenation of 2-chloro-2-phenylhexane. The alcohol which corresponded to this chloride was obtained from acetophenone and butyl bromide by the magnesium organic synthesis. In the hydrogenation of 9.45 g of the chloride we used 1096 ml of H_2 (771 mm, 23°) during 12 hours, which corresponded to 93%. We obtained 6 g of product of hydrogenation, from which we isolated about 4 g of 2-phenylhexane. B.p. 100-101° (20 mm), d_4^{20} 0.8608, nD^{20} 1.4868. The infrared spectrum is given in Fig. 1, curve 2.

3-Phenylhexane was obtained by hydrogenation of 3-chloro-3-phenylhexane. The corresponding alcohol was prepared from bromobenzene and ethylpropyl ketone by the magnesium organic synthesis. In the hydrogenation of 8.58 g of chloride we used 1112 ml of H_2 (770 mm, 22°) which corresponded to 94%. Distillation of the reaction product gave 3.5 g of 3-phenylhexane. B.p. 94.5-95° (20 mm), d_4^{20} 0.8617, nD^{20} 1.4870. The infrared spectrum is given in Fig. 1, curve 1.

The constants for the three phenylhexane isomers given in this paper are close to those given earlier in the literature [10].

Ozonolysis of 2-chloro-1-phenyl-3-hexyne. As a result of ozonization of 4.2 g of the substance during 7 hours and the usual treatment of the mixture, we obtained propionic acid with b.p. 51° (20 mm), nD^{20} 1.3889. Analysis of its silver salt (after recrystallization from water) was carried out.

Found %: C 21.38, 21.38; H 3.10, 3.13; Ag 60.45, 60.60. $C_5H_5O_2Ag$. Calculated %: C 19.91; H 2.78; Ag 59.66.

The residue after distillation of the propionic acid was recrystallized. M.p. 45-46° (from ligroin).

Found %: Cl 17.99, 17.80. $C_9H_9O_2Cl$. Calculated %: Cl 19.20.

Chlorophenylation of vinylisopropenylacetylene. From 24 g of vinylisopropenylacetylene and 17 g of aniline by the usual method we obtained 10.3 g of chloroarylation product.

B.p. 98-101° (1 mm), d_4^{20} 1.0265, nD^{20} 1.5744, MR 65.72; Calc. 61.03.

The infrared spectrum is given in Fig. 2, curve 6.

SUMMARY

1. We have studied the action of diazonium salts on vinylethyl- and vinylisopropenylacetylenes.

2. We have shown that the aryl radicals in all cases add to the end carbon atom, and in the case of vinylisopropenylacetylene preferably on the vinyl group.

3. We have shown that in distinction from vinylacetylene, vinylethylacetylene forms preferably 2-chloro-1-aryl-3-hexene; the allene isomer is obtained in considerably smaller amount.

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INFRARED ABSORPTION SPECTRA AND THE STRUCTURE OF SOME DERIVATIVES OF β-DIKETONES

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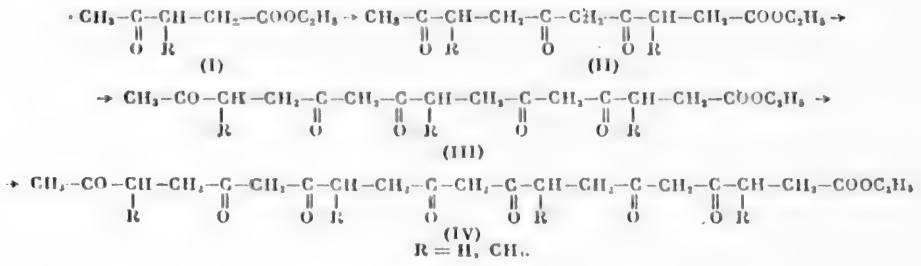
In order to establish the nature of the effect of lengthening the hydrocarbon chain which is contained as a repeating structural unit in β-diketone grouping $-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-$, we carried out a study of the infrared absorption spectra of some products of ester condensation of esters of levulinic acid (I, R = H) and β-methyllevulinic acid (I, R = CH_3).

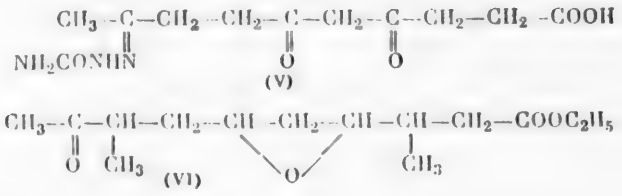


A number of investigations report the behavior of derivatives of β-diketones with respect to their ability to enolize and form metallic derivatives [1-6], but in most of them compounds were studied which had only one grouping $-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-$. The substances used in the present work were groups of compounds which had one, two, and three of such groupings, joined to each other by linear chains through two carbon atoms.

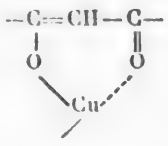
In the spectra of most β-diketones which have been studied there were wide, strong bands in the region of 1610 cm^{-1} whose presence is explained by a considerable degree of enolization with formation of a chelate hydrogen bond: $-\overset{\overset{O-H\ldots O}{|}}{C}=CH-\overset{\overset{O}{\|}}{C}-$. This band was assigned to a valence oscillation of the group C = O [2], and its unusually great shift compared to the "normal" position (1720 cm^{-1}) was explained: a) by conjugation with the double bond C = C, and b) the formation of the hydrogen bond which produces a six-membered chelate ring.

The result of condensation of ethyl levulinate and ethyl β-methyllevulinate with ethyl 4,6,9-triketocaprate (II, R = H) [7] and ethyl 3,8-dimethyl-4,6,9-triketocaprate (II, R = CH_3) [8] is to produce compounds which have the structure of substituted β-diketones. Their spectra in the region mentioned above show a marked absorption at 1620 cm^{-1}, which agrees with the position of analogous bands in acetylacetone (1615 cm^{-1}). This makes it possible to conclude that there is present in compounds (II, R = H, CH_3) a chelated enol form. The intensity of this band is slight, corresponding to (w) and (m), while the presence of an intense band at 1700 (s) cm^{-1} in (II, R = H) and 1720 (m) cm^{-1} in (II, R = CH_3) indicates the presence of a considerable quantity of the ketone form,and corresponding to this, alkaline titration of these compounds shows that the enol form amounts to about 30-40%. Also, esters of the triketocapric acids (II, R = H, CH_3) show two bands in the region 1735 (s) and 1775 (s) cm^{-1} which belong to the absorption of terminal isolated keto and ester groups respectively. The value of 1735 cm^{-1} is somewhat high for valence oscillation of an isolated keto group as compared to the generally accepted average of 1720 cm^{-1}; this increase is explained by the fact that the samples of these compounds studied were in the liquid state and not in solution. An analogous increase in frequency of valence oscillation of the C = O group in condensed samples as compared to solvents was noted earlier also in samples of other ketones [10].

In the spectrum of the monosemicarbazone of 4,6,9-triketocapric acid (V) the 1735 cm^{-1} band vanishes while the bands at 1775 (m) and 1700 (s) are kept. On the other hand, in the spectrum of compound (VI) obtained by hydrogenation of ethyl 3,8-dimethyl-4,6,9-triketocaprate (II, R = CH_3) in the presence of a skeletal nickel catalyst at 132-138° and 100 atm, the bands 1775 (m) and 1735 (s) remain while the bands 1720 and 1620 cm^{-1} disappear, which once more confirms the correctness of the interpretation of the spectra given above. In the absorption spectrum of compound (VI) we can see a strong band near 980 cm^{-1} which agrees in its position with the absorption of the cyclic oxide of trimethylene [11].



On further condensation of the ester (II, R = H) with ethyl levulinate we obtained the ethyl ester of 4,6,9,11,14-pentaketopentadecanoic acid (III, R = H) [12],which has two pairs of β-diketo groups. In an analogous way from substance (II, R = CH_3) we obtained the ethyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid [13]. With a divalent copper cation these compounds form enolates whose spectra show very strong absorption in the region 1620 (s) and 1560 (s) cm^{-1}. The intensity of absorption of the unbound C = O group in the keto form (1700-1735 cm^{-1}) is lowered markedly. Characteristic of the copper complexes of β-diketones are strong bands [1,4,6,14,15] in the region 1580-1560 cm^{-1} which can be related to the valence oscillation of the carbonyl group which occurs under the influence of a two fold decrease due to conjugation with the double bond C = C and formation of a chelate, here with the copper atom.



Thus the appearance of the strong band at 1560 cm^{-1} in the spectrum of the copper derivative of (III, R = H) indicates the formation of a stable copper chelate, and the presence in this spectrum in addition of the 1620 cm^{-1} band, which most naturally belongs to the valence oscillation of the C = C bond conjugated with the carbonyl group [2, 16], once more confirms the existence of this chelate. The absorption in the region 1700-1735 cm^{-1}, which, though greatly weakened, yet still remains, is due to the free keto and ester groups.

In the condensation of compound (II, R = H) with itself there is formed the ethyl ester of 4,6,9,11,14,16, 19-heptaketoicosanoic acid (IV, R = H),which already has three β-diketo groups. Its spectrum shows only slight

absorption in the region 1620 cm^{-1} (v.w.) (enol form), and at the same time it has bands at 1715 (s), 1740 (s), and 1775 (m) cm^{-1}, which, as in the previous interpretation of absorption in this region, can be assigned respectively to internal oscillation of the keto, terminal keto, and ester groups. Thus, from the absorption spectrum of compound (IV, R = H) it follows that in the free state the existence of the keto form is favored. However, determination of the molecular refraction of the substance (IV, R = H) in dioxane solution [12] (MR_D 109.00, calculated 108.7 for the enol form and 105.5 for the keto form) and the results of alkali titration (98.50% enol form) indicate the full enol form. Evidently here we are dealing with different conditions of existence of the molecule in the condensed state and in solution, where there can be a dynamic equilibrium between the two forms, so that a purely chemical process cannot give unchanged and definitive results [17].

The picture is changed with the formation of the copper complex of this compound. As in the case of compound (III, R = H) there are two strong bands 1620 (s) and 1570 (s) cm^{-1} which show the presence of chelate formation and the absorption in the region of the keto form (1700-1735 cm^{-1}) falls sharply while a weak band remains near 1720 cm^{-1} (v.w.). This fact recalls that in the previously studied chelates the oscillation of the double bond C = C conjugated with the C = O group was only slightly active in the infrared spectra. The absorption of the double bond, if it exists, is masked by the absorption of the bond C = O at 1610 cm^{-1} and also remains little noticed after the disappearance of this band in the formation of the copper chelate [1]. In our examples of the copper complexes of compounds (III and IV, R = H, CH_3) the double bond C = C in each case gives strong absorption at 1620 cm^{-1}; this fact can indicate in our case a difference in conditions of symmetry of the molecule as compared to the previously studied examples of β-diketones with single pairs of keto groups.

SUMMARY

1. We have studied the infrared absorption spectra of a series of substituted β-diketones which have one, two, and three β-diketo groupings, and also chelates of these compounds.

2. Lengthening the linear chain of β-diketo compounds does not permit their enolization, and in the free state favors the existence of their keto forms, although in solution the enol form can predominate.

3. The copper enolates of the ethyl esters of 4,6,9,11,14-pentaketopentadecanoic, 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic, 4,6,9,11,14,16,19-heptaketoicosanoic, and 3,8,13,18-tetramethyl-4,6,9,11,14,16,19-heptaketoicosanoic acids are clear chelate forms with characteristic frequencies in the region 1570-1560 cm^{-1}. Also in these compounds the valence oscillation of the C = C bond conjugated with the C = O group is active in the infrared spectrum and gives a strong band near 1620 cm^{-1}.

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THE SYNTHESIS OF ESTERS OF 3,8,13-TRIMETHYL-4,6,9,11,14-PENTAKETO-PENTADECANOIC AND 2,8,13,18-TETRAMETHYL-4,6,9,11,14,16,19-HEPTAKETOICOSANOIC ACIDS

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The condensation of esters of β-methyllevulinic acid (I, R = C_2H_5, CH_3) in the presence of 1 g-atom of sodium leads to the corresponding esters of 3,8-dimethyl-4,6,9-triketocapric acid (II, R = C_2H_5, CH_3) [1].

$$\underset{\text{(I)}}{CH_3COCHCH_2COOR} \rightarrow \underset{\text{(II)}}{CH_3COCHCH_2COCH_2COCHCH_2COOR}$$
$$\quad\quad\quad

Esters of substituted icosanoic acids were also obtained by reaction of esters of substituted pentadecanoic acids with esters of α-methyllevulinic acid.

$$(III) + CH_3COCH_2\underset{\underset{CH_3}{|}}{C}HCOOR \longrightarrow$$

(V)

$$CH_3COCHCH_2COCH_2COCHCH_2COCH_2COCHCH_2COCH_2COCH_2\underset{\underset{CH_3}{|}}{C}HCOOR$$

(VI)

In the reaction of the ethyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid (III, R = C_2H_5) with ethyl α-methyllevulinate (V, R = C_2H_5) we obtained the ethyl ester of 2,8,13,18-tetramethyl-4,6,9,11,14,16,19-heptaketoicosanoic acid (VI, R = C_2H_5). The reaction of condensation between the methyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid (III, R = CH_3) and ethyl α-methyllevulinate (V, R = C_2H_5) proceeds toward the formation of the ethyl ester of 2,8,13,18-tetramethyl-4,6,9,11,14,16,19-heptaketoicosanoic acid (VI, R = C_2H_5). Thus, it is evident in these cases that the acylating ester is the ester with more complex structure [the ethyl ester of 3,8-dimethyl-4,6,9,-triketocapric acid in obtaining compound (III, R = CH_3), and the methyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid in obtaining substance (VI, R = C_2H_5)].

All the above esters show reactions characteristic for β-diketones. The copper enolates of the esters have a chelate structure analogous to the corresponding enolates of the esters obtained from esters of levulinic acid [2]. The linear structure of the isolated esters was confirmed by determination of the number of methyl groups bound with carbon.

EXPERIMENTAL

Ethyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid (III, R = C_2H_5). To 0.89 g of sodium in the form of wire in 100 ml of absolute ether was added 6 g of ethyl β-methyllevulinate (b.p. 101-102° at 16 mm). On the next day the ester was decanted. The salt precipitate was carefully washed with ether. After drying over sodium sulfate, the solvent was removed. The residue (3.8 g) was distilled. Yield 1.65 g (37.5%).

B.p. 182-183° (0.15 mm), MR_D 96.70, calcd. 96.27 (for the keto form), 98.35 (for the enol form).

Found %: C 62.86, 62.94; H 7.78, 8.00; CH_3 10.5 (according to Kuhn-Roth), enol from 91 (by alkali titration), M 388 (cryoscopic method in dibromoethane). $C_{20}H_{30}O_7$. Calculated %: C 62.81, H 7.91, CH_3 23.3 (for five groups), M 382.2.

Methyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid (III, R = CH_3). a) In an analogous way from 15.2 g of methyl β-methyllevulinate and 2.44 g of sodium we obtained 11.3 g of technical methyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid. We distilled 2.5 g of the substance. Yield 0.9 g (37.9%). B.p. 179-181° (0.15 mm). From the remaining amount we obtained the copper enolate. M.p. 179-181°. After decomposition of the copper enolate by hydrogen sulfide we obtained 2.2 g (24.9%) of a substance in the form of a thick yellow oil.

MR_D 93.74; Calcd. 91.65 (for the keto form); 93.73 (for the enol form).

Found %: C 61.62; H 7.51; CH_3 10.2 (according to Kuhn-Roth); enol form 96 (alkaline titration), M 375. $C_{19}H_{28}O_7$. Calculated %: C 61.94, H 7.66, CH_3 16.2 (for four groups), M 368.4.

b) From 3 g of the ethyl ester of 3,8-dimethyl-4,6,9-triketocapric acid (b.p. 160-162° at 0.35 mm) and 1.58 g of methyl β-methyllevulinate in the presence of 0.5 g of sodium and 40 ml of anhydrous xylene we obtained 2.9 g of methyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid. After purification through the copper enolate we isolated 0.9 g (22%).

Found %: C 61.9, 61.93; H 7.76, 7.73. $C_{19}H_{28}O_7$. Calculated %: C 61.94; H 7.66.

Ethyl ester of 2,8,13,18-tetramethyl-4,6,9,11,14,16,19-heptaketoicosanoic acid (VI, R = C_2H_5). a) To 0.55 g of sodium in 30 ml of anhydrous xylene was added 2.2 g of the methyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid and 0.93 g of ethyl α-methyllevulinic acid (b.p. 78-79° at 6 mm). The reaction mass

was heated with stirring under reflux for 20 hours. The xylol was decanted, the precipitate of salt was washed with ether and dissolved in water. The solution was acidified with hydrochloric acid and extracted with ether. After drying with sodium sulfate the solvent was distilled off. The residue was a yellow oil (2 g). The copper enolate was precipitated. M.p. 190-191°. After decomposition of the copper enolate with hydrochloric acid we isolated 0.55 g of the substance (18.5%).

MR_D 127.65, Calcd. 127.14 (for the enol form).

Found %: C 63.44, 63.25; H 7.83, 7.85; CH_3 10.1 (according to Kuhn-Roth); enol form 89 (alkali titration). M 480. $C_{26}H_{38}O_9$. Calculated %: C 63.14; H 7.74; CH_3 21. M 494.56.

b) From 1.85 g of ethyl ester of 3,8,13-trimethyl-4,6,9,11,14-pentaketopentadecanoic acid and 0.75 g of ethyl α-methyllevulinate in the presence of 0.443 g of sodium in 40 ml of anhydrous xylene we obtained 1.9 g of condensation product. After distillation the yield was 0.4 g (16.6%). B.p. 179-182° (0.09 mm).

Found %: C 63.31; H 7.45. $C_{26}H_{38}O_9$. Calculated %: C 63.14; H 7.74.

Ethyl ester of 3,8,13,18-tetramethyl-4,6,9,11,14,16,19-heptaketoicosanoic acid (VI, R = C_2H_5). From 6.8 g of ethyl ester of 3,8-dimethyl-4,6,9-triketocapric acid and 1.15 g of sodium in anhydrous xylene we obtained 5.6 g of technical condensation product. The copper enolate was precipitated, m.p. 193-196°, from which hydrochloric acid gave 2.2 g (35.5%) of the ester (IV, R = C_2H_5).

MR_D 127.00; Calcd. 124 (for the keto form), 127.14 (for the enol form).

Found %: C 62.88, 63.33; H 7.67, 7.46; CH_3 9.8 (according to Kuhn-Roth); enol form 96 (alkali titration). $C_{26}H_{38}O_9$. Calculated %: C 63.14; H 7.74; CH_3 21.

SUMMARY

We have studied the Claisen condensation of esters of α- and β-methyllevulinic acids. We have shown that, depending on the amount of sodium, we can obtain different condensation products. Methyl β-methyllevulinate reacts more slowly than the corresponding ethyl ester. In the condensation of more complex esters (esters of substituted capric and pentadecanoic acids) with esters of α-methyllevulinic acid, acylation is by the esters with more complex structures.

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THE SYNTHESIS OF 3-METHYLHEXADECAN-1,16-DIOIC ACID

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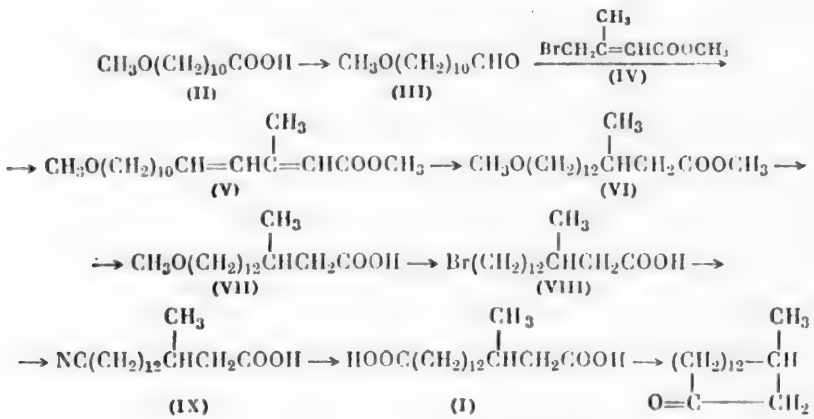
Aliphatic groups with the composition C_{16} and higher form the basis of a series of biologically active natural acids, macrocyclic ketones, lactones, and many other compounds [1]. In connection with our studies on the synthesis of higher aliphatic acids [2, 3] we have investigated the synthesis of 3-methylhexadecan-1,16-dioic acid (I), the chief intermediate in preparing muscone [4, 5].



11-Methoxyundecanal (III), obtained by reduction of 11-methoxyundecanoic acid (II) [6] by formic acid on a manganese aluminum catalyst, was condensed with the methyl ester of 4-bromo-3-methyl-2-butenoic acid (IV) with the aid of zinc and powdered copper [7]. The methyl ester of 4-bromo-3-methyl-2-butenoic acid (IV) used in the reaction was prepared by oxidation of mesityl oxide with an aqueous solution of potassium hypochlorite [8] followed by esterification and bromination with N-bromosuccinimide of the 3-methyl-2-butenoic acid.

The product of reaction of substances (III) and (IV) without separation and purification was dehydrated into the methyl ester of 15-methoxy-3-methylpentadeca-2,4-dienoic acid (V) and as a result of hydrogenation of this into compound (VI) and saponification of the latter we obtained 15-methoxy-3-methylpentadecanoic acid (VII). By the action of hydrogen bromide on compound (VII) the methoxy group was replaced by bromine, and the resulting 15-bromo-3-methylpentadecanoic acid (VIII) was converted with sodium cyanide into compound (IX), which was saponified into 3-methylhexadecandioic acid (I).

EXPERIMENTAL

11-Methoxyundecanal (III). Through a quartz tube containing 35 g of manganese-aluminum catalyst at

395-400° and at a rate of 20 ml/hour we passed a mixture of 130 g of 11-methoxyundecanoic acid (II) and 302.5 g of anhydrous formic acid. The resulting upper oily layer was separated and the lower layer was extracted with ether (3 × 100 ml). The combined extracts were neutralized with an aqueous solution of sodium bicarbonate and dried with sodium sulfate. After removal of the solvent, the residue was distilled. Yield 75.3 g (62.7%). B.p. 101-103°, m.p. 24.5-26°.

Found %: C 71.71; H 12.10. $C_{12}H_{24}O_2$. Calculated %: C 71.96; H 12.08.

Semicarbazone, m.p. 73-75° (from alcohol).

Found %: N 16.26. $C_{13}H_{27}O_2N_3$. Calculated %: N 16.32.

Methyl ester of 4-bromo-3-methyl-2-butenoic acid (IV). A solution of 95 g of N-bromosuccinimide (b.p. 172-175°), 56 g of methyl ester of 3-methyl-2-butenoic acid, and 0.2-0.3 g of benzoyl peroxide was heated to boiling for 5.5 hours. The solvent was removed, the precipitate was separated and washed with ether (2 × 50 ml). After removal of the solvent the residue was distilled. Yield 56.5 g (59.8%). B.p. 92-94° (11 mm).

Methyl ester of 15-methoxy-3-methylpentadeca-2,4-dienoic acid (V). A solution of 16 g of 11-methoxyundecanal (III) and 19.26 g of methyl ester of 4-bromo-3-methyl-2-butenoic acid (IV) in 20 ml of toluene was added to a mixture of 8 g of activated zinc, 0.8 g of copper powder, and 30 ml of anhydrous boiling toluene. Then the reaction mixture was heated for one hour, cooled to 18-20°, 50 ml of 10% acetic acid was added and the unreacted zinc and copper were filtered off. From the mother liquors the upper layer was separated and from the water layer the substance was removed by toluene (3 × 75 ml). The combined extracts were neutralized with an aqueous suspension of sodium bicarbonate. The solvent was removed and the residue (15.1 g) was added over a period of 30 minutes to a boiling mixture of 6 ml of phosphorus oxychloride, 25 ml of benzene, and 22 ml of pyridine. The reaction mass was heated at the boiling point for one hour, then cooled to 18-20°, poured onto 100 g of ice, and the upper layer separated; from the water layer the substance was removed with benzene (3 × 100 ml). The combined extracts were dried with sodium sulfate. After removal of the solvent, the residue was distilled. Yield 10.7 g [45% calculated on 11-methoxyundecane (III)].

B.p. 167-170° (0.4 mm), d_4^{20} 0.9515, nD^{20} 1.4769, MR 88.06; Calc. 87.69.

Found %: C 73.22; H 10.50. $C_{16}H_{32}O_3F_2$. Calculated %: C 72.95; H 10.88.

Methyl ester of 15-methoxy-3-methylpentadecanoic acid (VI). A solution of 19.56 g of the methyl ester of 15-methoxy-3-methylpentadeca-2,4-dienoic acid (V) was hydrogenated in an autoclave at 29-35° for five hours in the presence of a nickel catalyst (the initial hydrogen pressure was 135 atm). The catalyst was separated from the reaction mass and washed with alcohol (2 × 14 ml). After removal of the solvent the residue was distilled. Yield 14.42 g (72.9%).

B.p. 138-141° (0.4 mm), d_4^{20} 0.9048, n_D^{20} 1.4778, MR 88.86; Calc. 88.62.

Found %: C 72.10; H 11.75. $C_{18}H_{36}O_3$. Calculated %: C 71.94; H 12.08.

15-Methoxy-3-methylpentadecanoic acid (VII). A mixture of 18 ml of a 10% potassium hydroxide solution in methanol and 14.42 g of the methyl ester of 15-methoxy-2-methylpentadecanoic acid (VI) was heated to boiling for five hours, the excess solvent was distilled off, and 100 ml of water was added. Unsaponified compound (VI) was removed with ether (3 × 50 ml) and the water layer was acidified with hydrochloric acid (d_4^{20} 1.10) and the substance was extracted with ether (2 × 100 ml). The combined extracts were dried with sodium sulfate. After removal of the solvent, the residue was distilled. Yield 9.3 g (67.8%).

B.p. 178-179° (0.7 mm), d_4^{20} 0.9351, nD^{20} 1.4599, MR 83.85; Calc. 83.87.

Found %: C 71.33; H 12.10. $C_{17}H_{34}O_2$. Calculated %: C 71.29; H 11.96.

15-Bromo-3-methylpentadecanoic acid (VIII). Through a solution of 3.93 g of 15 methoxy-3-methylpentadecanoic acid (VII) in 50 ml of glacial acetic acid at 20-22° for ten hours was passed hydrogen bromide. Then, without stopping passage of the gas, the temperature of the reaction mass was gradually raised to 100°, heating was continued under these conditions for fifteen hours, and 150 ml of water was added. The lower layer was separated and from the upper the substance was extracted with chloroform (3 × 50 ml). The combined extracts were neutralized with a saturated water solution of sodium bicarbonate to pH 4. After removal of the solvent, the residue was distilled. Yield 3.11 g (67.6%).

B.p. 189-190.5° (0.5 mm), d_4^{20} 1.1230, nD^{20} 1.4852, MR 85.32; Calc. 85.39.

Found %: C 57.48; H 9.23; Br 23.85. $C_{16}H_{31}O_2Br$. Calculated %: C 57.31; H 9.32; Br 23.83.

15-Cyano-3-methylpentadecanoic acid (IX). To a solution of 1.1 g of sodium cyanide in 4 ml of water was added 3.02 g of 15-bromo-3-methyl-pentadecanoic acid (VIII) and 22 ml of alcohol. The mixture was heated to boiling for 30 hours. Then the solvent was distilled off, the residue was dissolved in 10 ml of water, acidified with sulfuric acid (d_4^{20} 1.40) to pH 5, and the reaction product was extracted with chloroform (2 × 50 ml). The resulting extract was dried with sodium sulfate. After removal of the solvent, the residue was distilled. Yield 1.96 g (77.5%).

B.p. 193-194° (0.35 mm), d_4^{50} 0.9422, nD^{50} 1.4647, MR_D 82.54; Calc. 82.06.

Found %: C 72.54; H 11.30; N 5.32. $C_{17}H_{31}O_2N$. Calculated %: C 72.51; H 11.11; N 4.97.

3-Methylhexadecan-1,16-dioic acid (I). A mixture of 1.5 g of potassium hydroxide in 1 ml of water and 1.38 g of 15-cyano-3-methylpentadecanoic acid (IX) in 1 ml of alcohol was heated to boiling for 35 hours. The unsaponified nitrile (IX) was extracted with 10 ml of ether, the residue was dissolved in 10 ml of water, neutralized with sulfuric acid (d_4^{20} 1.40) and the reaction product was extracted with ether (2 × 25 ml). After removal of the solvent the residue was distilled. Yield 1.26 g (85.4%). B.p. 111-112° (0.45 mm), m.p. 78-79.5°.

Found %: C 67.72; H 10.53. $C_{17}H_{32}O_4$. Calculated %: C 67.95; H 10.74.

SUMMARY

1. We have carried out the synthesis of 3-methylhexadecan-1,16-dioic acid, a basic intermediate in the preparation of muscone.

2. In the course of the synthesis we have isolated and characterized the methyl ester of 15-methoxy-3-methylpentadeca-2,4-dienoic acid, the methyl ester of 15-methoxy-3-methylpentadecanoic acid, 15-methoxy-3-methylpentadecanoic acid, 15-bromo-3-methylpentadecanoic acid, and 15-cyano-3-methylpentadecanoic acid.

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THE SYNTHESIS OF 1,1-ETHYLENEDIOXY-5-HEXYNE

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In the molecule of arachidonic acid (I) between the carboxyl group and the double bond nearest to it there are three methylene groups.

$$C_5H_{11}(CH_2CH{=}CH)_4CH_2CH_2CH_2COOH \ (I)$$

In this paper we describe the preparation of 1,1-ethylenedioxy-5-hexyne (II), one of the starting substances in the synthesis of arachidonic acid [1, 2] (I).

$$HC{\equiv}CCH_2CH_2C{\equiv}CH \ (III) + CH_3COSH \ (IV) \longrightarrow HC{\equiv}CCH_2CH_2CH{=}CHSCOCH_3 \ (V) \longrightarrow$$
$$\longrightarrow HC{\equiv}CCH_2CH_2CH_2CH{=}NOH \ (VI) \longrightarrow [HC{\equiv}CCH_2CH_2CH_2CHO] \ (VII) \longrightarrow$$
$$\longrightarrow HC{\equiv}CCH_2CH_2CH_2CH\begin{matrix}OCH_2\\|\\OCH_2\end{matrix} \ (II)$$

In the reaction of dipropargyl (III) [3] with thioacetic acid (IV) [4, 5] there is formed the vinylthiol ester (V). Treatment of the thioester (V) with hydroxylamine hydrochloride in the presence of sodium acetate leads to the 5-hexynaldoxime (VI). By the action on the oxime (VI) of butyl nitrite there is obtained the corresponding aldehyde (VII) which with ethylene glycol is transformed into the cyclic acetal (II). 1,1-Ethylenedioxy-5-hexyne (II) does not have a characteristic absorption in the ultraviolet, and its infrared spectrum shows the presence of a monosubstituted triple bond.

EXPERIMENTAL

1. 1-Hexen-5-yn-1-thiol acetate (V). To 16.2 g of dipropargyl (III) (b.p. 87-88.5° at 752 mm) was added 15 g of thioacetic acid (IV) (b.p. 87-89° at 757 mm); the solution became warm. The mixture was boiled for one hour and at a constantly increasing temperature of the bath to 130° the unreacted starting substances were distilled off (5.3 g). The residue was distilled. Colorless liquid with a characteristic odor. Yield 8.1 g (26.7%).

B.p. 89-91° (6 mm), d_4^{20} 1.048, nD^{20} 1.5209, MR_D 44.75. $C_8H_{10}OS$ EF. Calculated 44.69.

Found %: C 62.51; 62.20; H 6.58; 6.43. $C_8H_{10}OS$. Calculated %: C 62.31; H 6.53.

2. 5-Hexynaldoxime (VI). To 6.21 g of the thiol acetate (V) at 3-5° was added a solution of 5.57 g of hydroxylamine hydrochloride and 10.88 g of sodium acetate (trihydrate) in 100 ml of 96% alcohol and 10 ml of water. The temperature rose to 35-40°, hydrogen sulfide was evolved, and a mineral residue precipitated. The reaction

mass was heated to boiling for six hours, the residue was separated, and the solvent was removed in a vacuum. To the residue was added 20 ml of water and it stood over night at 2-3°. The precipitate was separated, distilled, and recrystallized from water. Colorless crystals. B.p. 82-84° (5 mm), m.p. 72-73.5°. Yield 3.30 g (74.4%).

Found %: N 12.47, 12.38. C_6H_9ON. Calculated %: N 12.61.

3. 1,1-Ethylenedioxy-5-hexyne (II). To a mixture of 10 ml of ethylene glycol, 1 ml of water, and 0.1 ml of concentrated sulfuric acid with stirring and cooling to -10 to -5° was added by turns in small portions over 40 minutes 3.22 g of butyl nitrite and 3.20 g of hexynaldoxime (VI). After 15 minutes of stirring the reaction mass became homogeneous. We added 20 ml of ethylene glycol, 100 ml of anhydrous benzene, and the water (1.9 ml) was removed by azeotropic distillation. The mixture was cooled to 20°, diluted with 100 ml of 5% sodium hydroxide solution, the benzene layer was separated, and the water was extracted with ether (2 × 20 ml). The combined extracts were washed with water (2 × 10 ml) and dried over sodium sulfate. The solvent was removed and the residue was distilled. Colorless liquid with an ethereal odor. Yield 2.19 g (52.4%). Infrared spectrum: 3310 cm^{-1}, 2120 (m) cm^{-1}.

B.p. 86-88° (14 mm), d_4^{20} 0.9957, nD^{20} 1.4516. MR_D 38.15. $C_8H_{12}O_2F$. Calculated 38.23.

Found %: C 68.23, 68.38; H 8.75, 8.73. $C_8H_{12}O_2$. Calculated %: C 68.55; H 8.63.

2,4-Dinitrophenylhydrazone, m.p. 97-98° (from alcohol).

Found %: N 20.16, 20.54. $C_{12}H_{12}O_4N_4$. Calculated %: N 20.29.

SUMMARY

We have carried out the synthesis of 1,1-ethylenedioxy-5-hexyne through a series of steps.

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HOFMANN CLEAVAGE OF 1-AZABICYCLO[3.2.1]OCTANES

III. HOFMANN CLEAVAGE OF THE QUATERNARY BASE 2-METHYL-1-AZABICYCLO[3.2.1]OCTANE

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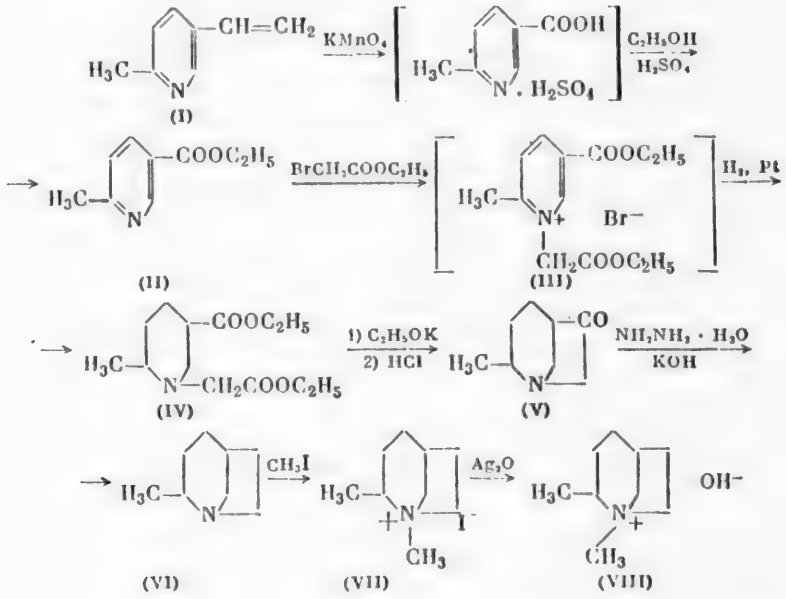
In previous communications [1, 2] we have presented data relating to the Hofmann cleavage of the quaternary bases 1-azabicyclo[3.2.1]octane and 7-methyl-1-azabicyclo[3.2.1]octane. It has been established that the cleavage of 1-azabicyclo[3.2.1.]octane goes in different ways depending on the conditions, while the cleavage of 7-methyl-1-azabicyclo[3.2.1]octane goes in only one way.

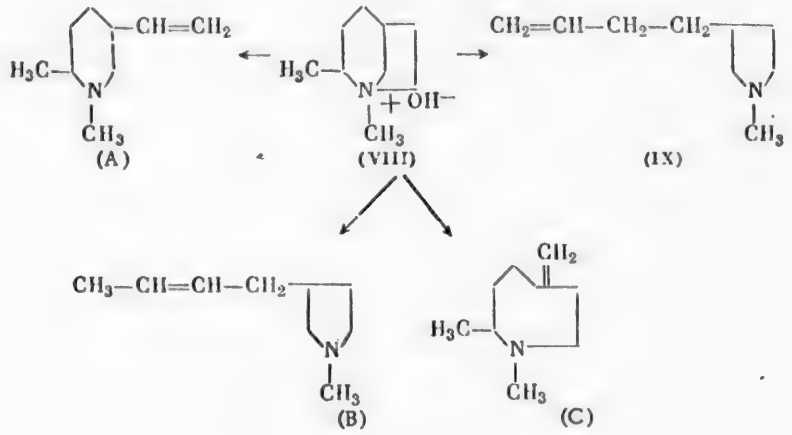
The present work is a continuation of the investigations mentioned and reports data obtained in the cleavage of 2-methyl-1-azabicyclo[3.2.1]octane. This compound was prepared from 2-methyl-5-vinylpyridine according to the following scheme:



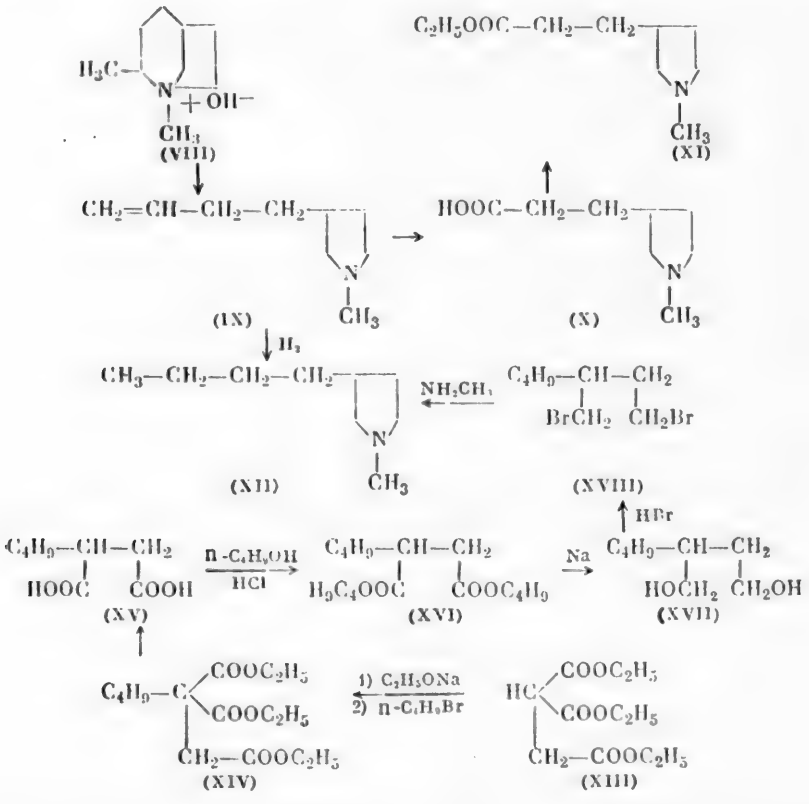
2-Methyl-5-vinylpyridine (I) was oxidized with potassium permanganate to 2-methylpyridine-5-carboxylic acid, which was esterified without isolation to ethyl 2-methylpyridine-5-carboxylate (II). The 1-carboethoxymethyl-2-methyl-5-carboethoxypyridinium bromide (III) that was produced by the reaction of the ester (II) with ethyl bromoacetate was reduced in the presence of Adams platinum catalyst to 1-carboethoxymethyl-2-methyl-5-carboethoxypyridine (IV). Intramolecular condensation of the diester (IV) with formation of 2-methyl-1-azabicyclo[3.2.1]octanone-6 (V) was carried out in toluene solution with the aid of potassium alcoholate. When the ketone

(V) was reduced by the Kizhner method [3], 2-methyl-1-azabicyclo [3.2.1] octane (VI) was obtained, which was converted by the action of methyl iodide to the quaternary salt (VII), and then with the aid of silver oxide to the corresponding quaternary base (VIII).

By Hofmann cleavage of the base (VIII) it is theoretically possible to produce the four compounds (A), (B), (C), and (IX), and also their hydration products.



We have studied the cleavage of the base (VIII) under various conditions: heating in vacuum, at atmospheric pressure, under pressure in a sealed tube, and also heating in the presence of 40% potassium hydroxide solution at atmospheric pressure. Under all the conditions mentioned, the same compound was isolated in 62-85% yield; this compound contained a double bond and according to data from its analysis it had the composition $C_9H_{17}N$.



When this unsaturated compound was oxidized with potassium permanganate, a material was obtained which contained a carboxyl group, thus excluding the structure of compound (C), oxidation of which would lead to a ketone. The hydrochloride of the oxidation product gave a depression in melting point when mixed with a sample of the hydrochloride of 1-methylpyrrolidyl-3-acetic acid [1]. The latter should be formed by the oxidation of the compound with structure (B).

Reduction of the unsaturated cleavage product yielded a compound identical with 1-methyl-3-butylpyrrolidine (XII) synthesized by us by the scheme shown below. Thus, the unsaturated product of the cleavage of the quaternary base 2-methyl-1-azabicyclo [3.2.1] octane was 1-methyl-3-(butene-3',4')-pyrrolidine (IX).

1-Methyl-3-butylpyrrolidine was prepared starting with the diethyl ester of carboethoxysuccinic acid (XIII). Compound (XIII) was alkylated with the aid of n-butyl bromide in the presence of sodium alcoholate. From the diethyl ester of 1-butyl-1-carboethoxysuccinic acid (XIV) which was produced, we obtained by prolonged heating with concentrated hydrochloric acid 1-butylsuccinic acid (XV), the dibutyl ester of which (XVI) was reduced with the aid of metallic sodium in butyl alcohol to 2-butyl-1,4-tetramethylene glycol (XVII). The latter was converted by reaction with 64% hydrobromic acid to 2-butyl-1,4-dibromobutane (XVIII). When the bromide (XVIII) was condensed with methylamine, we obtained 1-methyl-3-butylpyrrolidine, the boiling point and refractive index of which agreed with the corresponding constants for compound (XII), prepared by reduction of the cleavage product (IX). Furthermore, the identity of compound (XII) with the 1-methyl-3-butylpyrrolidine synthesized was confirmed by the absence of a depression in melting point when samples of their picrates were mixed.

EXPERIMENTAL

Ethyl 2-methylpyridine-5-carboxylate (II). To a solution of 30 g of 85% 2-methyl-5-vinylpyridine in 300 ml of 10% sulfuric acid there was added, with stirring, over a period of 4 hours, 133 g of potassium permanganate in the form of a 4% aqueous solution, while the temperature of the reaction mixture was maintained at not higher than 5°. After addition of the oxidizing agent, stirring was continued for 2 hours at the same temperature. Then the manganese dioxide was filtered out and washed with hot water. The combined aqueous solutions were acidified with sulfuric acid to a weak acid reaction to congo and were evaporated on a water bath. The residue, consisting of the sulfate of 2-methylpyridine-5-carboxylic acid and potassium sulfate was dried to constant weight in a vacuum desiccator over sulfuric acid, then mixed with 100 ml of anhydrous alcohol and 33 ml of concentrated sulfuric acid and boiled for 3 hours. The cooled reaction mixture was poured over ice and neutralized with dry sodium carbonate. The inorganic salts were filtered off and the filtrate was extracted repeatedly with chloroform. The extract was dried with potassium carbonate, the chloroform was distilled off, and the residue was distilled. Nineteen grams (54%) of ethyl 2-methylpyridine-5-carboxylate was obtained. Colorless, mobile liquid with b.p. 144-145° (45 mm), nD^{20} 1.5013.

Found %: C 65.76; H 6.83; N 8.69. $C_9H_{11}O_2N$. Calculated %: C 65.45; H 6.67; N 8.45.

1-Carboethoxymethyl-2-methyl-5-carboethoxypiperidine (IV). A solution of 80 g of ethyl 2-methylpyridine-5-carboxylate (II) and 90 g of ethyl bromoacetate in 35 ml of anhydrous alcohol was heated for 4 hours at 60-70° and left overnight at room temperature. The caramel-like mass obtained, which was 1-carboethoxymethyl-2-methyl-5-carboethoxypyridinium bromide (III), was dissolved in 600 ml of anhydrous alcohol and subjected to catalytic reduction in the presence of 0.8 g of Adams platinic oxide. After the required amount of hydrogen (36.5 liters) had been absorbed, the platinum black was filtered off, the filtrate was evaporated in vacuum, and the residue was treated, while being cooled, with an excess of 50% potassium carbonate solution and extracted with ether. The extract was dried with potassium carbonate, and the ether was distilled off in vacuum. One hundred grams (80%) of 1-carboethoxymethyl-2-methyl-5-carboethoxypiperidine was obtained as a colorless oil with b.p. 167-168° (15 mm), nD^{20} 1.4582. It was not possible to crystallize the hydrochloride.

Found %: C 60.49; H 8.94; N 5.74. $C_{13}H_{23}O_4N$. Calculated %: C 60.75; H 8.95; N 5.45.

2-Methyl-1-azabicyclo [3.2.1] octanone-6 (V). To a suspension of 32 g of metallic potassium in 100 ml of toluene was added gradually, with stirring, a solution of 50 ml of anhydrous alcohol in 50 ml of anhydrous toluene. The reaction mixture was boiled for 2 hours. To the potassium alcoholate that was produced was added over the course of 1 hour a solution of 80 g of 1-carboethoxymethyl-2-methyl-5-carboethoxypiperidine in 150 ml of anhydrous toluene, while uniform boiling of the mixture was maintained. After the addition of the diester, the

reaction mixture was boiled for 5 hours. Then 400 ml of concentrated hydrochloric acid was carefully added, with cooling and stirring, and the toluene layer was separated and washed with 400 ml of concentrated hydrochloric acid. The combined hydrochloric acid solution was boiled for 15 hours, decolorized with activated carbon, and evaporated on a steam bath. The residue was treated, with cooling, with an excess of 50% potassium hydroxide solution. The potassium chloride was filtered off and washed with a small amount of ice water and ether. The mother liquor was carefully extracted with ether. The ether extract was dried with potassium carbonate. The ether was distilled off in vacuum and the residue was distilled. Thirty and five-tenths grams (72%) of the ketone was obtained as a colorless oil with b.p. 105° (17 mm), nD^{20} 1.4869.

Picrate, yellow crystals, m.p. 232° (from alcohol).

Found %: C 45.37; H 4.41; N 15.49. $C_{14}H_{16}O_8N_4$. Calculated %: C 45.65; H 4.35; N 15.23.

2-Methyl-1-azabicyclo [3.2.1]octane (VI). Eight grams of 2-methyl-1-azabicyclo [3.2.1]octanone-6 (V), 12 g of pure potassium hydroxide, 8 ml of hydrazine hydrate, and 80 ml of anhydrous glycerol were heated slowly (foaming was possible) to 165-170° (in the bath) and kept at this temperature for 5 hours. Then the 2-methyl-1-azabicyclo [3.2.1]octane (VI) was distilled off from the reaction mixture, while the temperature was raised gradually to 250°. The distillate was extracted with ether, the ether extract was dried with potassium carbonate and evaporated, and the residue was distilled. Five and five-tenths grams (72%) of 2-methyl-1-azabicyclo [3.2.1]-octane was obtained as a colorless oil with a sharp amine odor. B.p. 165-166°, nD^{20} 1.4734.

Found %: N 11.54. $C_8H_{15}N$. Calculated %: N 11.20.

Picrate, yellow, needle-like crystals, m.p. 272° (from alcohol).

Found %: C 47.45; H 5.03; N 15.47. $C_{14}H_{18}O_7N_4$. Calculated %: C 47.45; H 5.09; N 15.82.

Methiodide, white, needle-like crystals, m.p. 316-318° (from alcohol).

Found %: N 5.27; I 47.48, 47.64. $C_9H_{18}NI$. Calculated %: N 5.24; I 47.56.

Hofmann cleavage of 2-methyl-1-azabicyclo [3.2.1]octane under various conditions. A solution of 10 g of 2-methyl-1-azabicyclo [3.2.1]octane methiodide in 50 ml of distilled water was shaken for 5 hours with moist silver oxide prepared from 10 g of silver nitrate. The silver iodide and the excess silver oxide were filtered off and washed with distilled water and the combined filtrate was evaporated in vacuum at 50-60° (bath temperature). The residual oil, which was the quaternary base (VIII), was transferred to a Wurtz flask and heated at atmospheric pressure to 200° (bath temperature). At 140° decomposition began, accompanied by vigorous effervescence and distillation of the decomposition products. The distillate was extracted with ether, the ether extract was dried with potassium carbonate, the ether was distilled off, and the residue was distilled. Four grams (77%) of 1-methyl-3-(butene-3',4')-pyrrolidine was obtained as a colorless, mobile liquid with a sharp amine odor, readily soluble in organic solvents and poorly soluble in water. The compound contained a double bond. B.p. 170-172°, nD^{20} 1.4518.

Picrate, yellow crystals in the form of needles, m.p. 103-105° (from alcohol).

Found %: C 49.02, H 5.34; N 15.10. $C_{15}H_{20}O_7N_4$. Calculated %: C 48.91; H 5.44; N 15.22.

When the quaternary base 2-methyl-1-azabicyclo [3.2.1]octane was heated in vacuum (50-55 mm) under pressure in a sealed tube (190-200°) and in the presence of alkali at atmospheric pressure, in all cases 1-methyl 3-(butene-3',4')-pyrrolidine was isolated in yields of 81, 62, and 85%, respectively.

Ethyl β-(1-methylpyrrolidyl-3)-propionate (XI). Two grams of 1-methyl-3-(butene-3',4')pyrrolidine was oxidized under the conditions described above for the preparation of ethyl 2-methylpyridine-5-carboxylate. The mixture of the sulfate of the acid and potassium sulfate obtained as a result of the oxidation was treated with an excess of 50% potassium carbonate solution and extracted with ether.

Ketones were not detected in the extract. The alkaline solution was acidified with sulfuric acid, evaporated in vacuum, and the residue was dried to constant weight. The sulfate of the acid was extracted with hot alcohol, the alcohol was evaporated, and the residue was boiled with 10 times its amount of 4% alcoholic solution of hydrogen chloride for 3 hours. Then the alcohol was distilled off and the residue was treated with an excess of 50% potassium carbonate solution and extracted with ether. After the extract had been dried and the solvent distilled off, the residue was distilled. One and three-tenths grams (50%) of ethyl β-(1-methylpyrrolidyl-3)-propionate was obtained with b.p. 133-134° (35 mm), nD^{20} 1.4478.

Found %: N 7.79, 7.68. $C_{10}H_{19}O_2N$. Calculated %: N 7.58.

Picrate, yellow crystals, m.p. 111-112° (from alcohol).

Found %: C 46.19; H 5.02; N 13.54. $C_{16}H_{22}O_9N_4$. Calculated %: C 46.32; H 5.32; N 13.53.

β-(1-Methylpyrrolidyl-3)propionic acid hydrochloride (X). Eight-tenths gram of the ethyl ester (XI) and 10 ml of hydrochloric acid (1:1) were boiled for 4 hours. The hydrochloric acid solution was decolorized with activated carbon and evaporated in vacuum. The residue, which was a caramel-like mass, crystallized when it was triturated with dry acetone. Seven-tenths gram (81%) of β-(1-methylpyrrolidyl-3)-propionic acid hydrochloride was obtained. White crystalline powder, readily soluble in water and alcohol, insoluble in ether and acetone, with m.p. 105-107° (from a mixture of alcohol and acetone). A mixed sample with (1-methylpyrrolidyl-3)-acetic acid hydrochloride (m.p. 95-97° [1]) melted at 72-76°.

Found %: C 49.46; H 8.50; N 7.43; Cl 18.20. $C_8H_{15}O_2N \cdot HCl$. Calculated %: C 49.60; H 8.28; N 7.24; Cl 18.34.

1-Methyl-3-butylpyrrolidine (XII). To a solution of 1 g of 1-methyl-3-(butene-3',4')-pyrrolidine (IX) in 50 ml of anhydrous alcohol were added 2 ml of a 25% alcoholic solution of hydrogen chloride and 0.15 g of platinic oxide. The hydrogenation was carried out at room temperature. After 1 mole of hydrogen had been absorbed, the platinum black was filtered off and the alcohol was distilled off in vacuum. The residue was treated with an excess of 50% potassium carbonate solution and extracted with ether. The ether extract was dried with potassium carbonate, evaporated, and the residue was distilled at atmospheric pressure. Seven-tenths gram (70%) of 1-methyl-3-butylpyrrolidine was obtained as a colorless oil with a sharp amine odor. The compound was readily soluble in organic solvents, poorly soluble in water. B.p. 170-172°, nD^{20} 1.4368.

Found %: N 10.03. $C_9H_{19}N$. Calculated %: N 9.93.

Picrate, yellow crystals in the form of needles, m.p. 134-135° (from alcohol).

Found %: C 48.75; H 5.81; N 14.91. $C_{15}H_{22}O_7N_4$. Calculated %: C 48.65; H 5.94; N 15.14.

Diethyl ester of 1-butyl-1-carboethoxysuccinic acid (XIV). To the alcoholate prepared from 4.7 g of sodium and 50 ml of anhydrous alcohol was added 50 g of the diethyl ester of 1-carboethoxysuccinic acid [4] at 20°. Then the reaction mixture was boiled for 1 hour, cooled, and 29 g of butyl bromide was added and the mixture was heated on a boiling water bath until the alkaline reaction to litmus disappeared (18 hours). After the mixture had cooled, 60 ml of water was added, the precipitate of sodium bromide was dissolved, and the oil layer was separated and extracted with ether. The ether extract was dried with sodium sulfate. After removal of the ether and distillation of the residue in vacuum, 46 g (74%) of the diethyl ester of 1-butyl-1-carboethoxysuccinic acid was obtained with b.p. 164-166° (17 mm).

Found %: C 59.74; H 8.66. $C_{15}H_{26}O_6$. Calculated %: C 59.60; H 8.61.

1-Butylsuccinic acid (XV). A mixture of 43 g of the ester (XIV) and 430 ml of concentrated hydrochloric acid was refluxed for 30 hours. The hydrochloric acid solution was evaporated in vacuum and the residue was recrystallized from water. Eighteen grams (73.7%) of butylsuccinic acid was obtained with m.p. 81° (from water).*

Foudn %: C 55.22; H 8.03. $C_8H_{14}O_4$. Calculated %: C 55.17; H 8.04.

Dibutyl ester of butylsuccinic acid (XVI). A solution of 18 g of butylsuccinic acid in 180 ml of anhydrous butyl alcohol was saturated in the cold with hydrogen chloride. Then the reaction mixture was boiled for 3 hours. The alcohol was distilled off in vacuum, the residue was stirred with 300 ml of ice water, the oil that separated out was removed and washed three times with ice water, then with a 6% solution of sodium bicarbonate, and again 2-3 times with ice water. It was dried with sodium sulfate and distilled. Twenty-five grams (84%) of the dibutyl ester of butylsuccinic acid was obtained with b.p. 200-202° (40 mm).

Found %: C 67.47; H 10.64. $C_{16}H_{30}O_4$. Calculated %: C 67.13; H 10.49.

* 1-Butylsuccinic acid was prepared previously by reduction of butylmaleic or butylfumaric acid with sodium amalgam. M.p. 81° (from water) [5].

2-Butyl-1,4-tetramethylene glycol (XVII). To a solution of 23 g of the dibutyl ester (XVI) in 300 ml of anhydrous butyl alcohol was added 19.3 g of sodium cut into coarse pieces. The mixture was boiled for 1.5 hours. In the course of this time the sodium dissolved. To the cooled solution was added 25 ml of distilled water and the mixture was boiled for 1.5 hours. After the mixture had cooled, 120 ml of distilled water was added, the oily layer was separated and washed 3 times with a small amount of water, and the combined aqueous solution was extracted with chloroform. The chloroform extract was combined with the oil and dried with sodium sulfate. The chloroform was distilled off and the residue was distilled. Six and five-tenths grams (55.6%) of 2-butyl-1,4-tetramethylene glycol was obtained as a colorless oil with b.p. 142-143° (10 mm), nD^{20} 1.4522.

Found %: C 65.41; H 12.22. $C_8H_{18}O_2$. Calculated %: C 65.75; H 12.33.

2-Butyl-1,4-dibromobutane (XVIII). A mixture of 5.5 g of the glycol (XVII) and 20 ml of 64% hydrobromic acid was heated in a sealed tube at 100° for 5 hours. The reaction mixture was extracted with ether, the ether extract was washed with water, then with 6% solution of sodium bicarbonate, and again with water. Then it was dried with sodium sulfate, and after removal of the ether, the residue was distilled. Four and five-tenths grams (45%) of 2-butyl-1,4-dibromobutane was obtained. Colorless liquid with b.p. 125-127° (12 mm), nD^{20} 1.4927.

Found %: Br 57.81. $C_8H_{16}Br_2$. Calculated %: Br 58.82.

1-Methyl-3-butylpyrrolidine (XII). A mixture of 4 g of 2-butyl-1,4-dibromobutane (XVIII) and 20 ml of 33% aqueous solution of methylamine was heated in a sealed tube for 5 hours at 190-200° (bath temperature). The reaction mixture was made alkaline and extracted with ether. The ether solution was dried with potassium carbonate, evaporated, and the residue was distilled. One gram (50%) of 1-methyl-3-butylpyrrolidine (XII) was obtained with b.p. 170-172°, nD^{20} 1.4368.

Found %: N 10.12. $C_9H_{19}N$. Calculated %: N 9.93.

Picrate, yellow crystals in the form of needles with m.p. 134-135° (from alcohol).

Found %: C 48.51; H 5.81; N 15.14. $C_{15}H_{22}O_7N_4$. Calculated %: C 48.65; H 5.94; N 15.14.

The picrate did not give a depression in melting point when mixed with the picrate of 1-methyl-3-butylpyrrolidine (XII), prepared by reducing 1-methyl-3-(butene-3',4')-pyrrolidine, the product of the Hofmann cleavage of the quaternary base 2-methyl-1-azabicyclo[3.2.1]octane (VIII).

SUMMARY

It has been established that Hofmann cleavage of 2-methyl-1-azabicyclo[3.2.1]octane under various conditions goes in one direction with the formation of 1-methyl-3-(butene-3',4')-pyrrolidine.

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*Original Russian pagination. See C. B. Translation.

INFRARED ABSORPTION SPECTRA OF PIAZSELENOLE AND A NUMBER OF ITS DERIVATIVES

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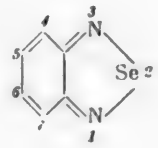
It has been reported previously that one can refer piazselenole (I).



(I)

to the condensed systems in which the equivalence of the bonds in the benzene ring is disrupted [1], accompanied, in our opinion [2-4], by the formation of an o-quinoid ring as a structural element of the molecule. It seemed of interest to ascertain how such a disruption of the equivalence of the bonds of the benzene ring is manifested in the infrared absorption spectra.

EXPERIMENTAL

The compounds investigated were: piazselenole (I), m.p. 76°, b.p. 246° (765 mm), d^{80} 1.770; piazselenole derivatives: 5-methyl- (II), m.p. 73-73.5°; 4-methyl- (III), m.p. 110.6-111.2°; 5-amino- (IV), m.p. 149-150°; 4-amino- (V), m.p. 159-159.7°; 5-nitro- (VI), m.p. 220-220.5°; 4-nitro- (VII), m.p. 216.5-217.3°.

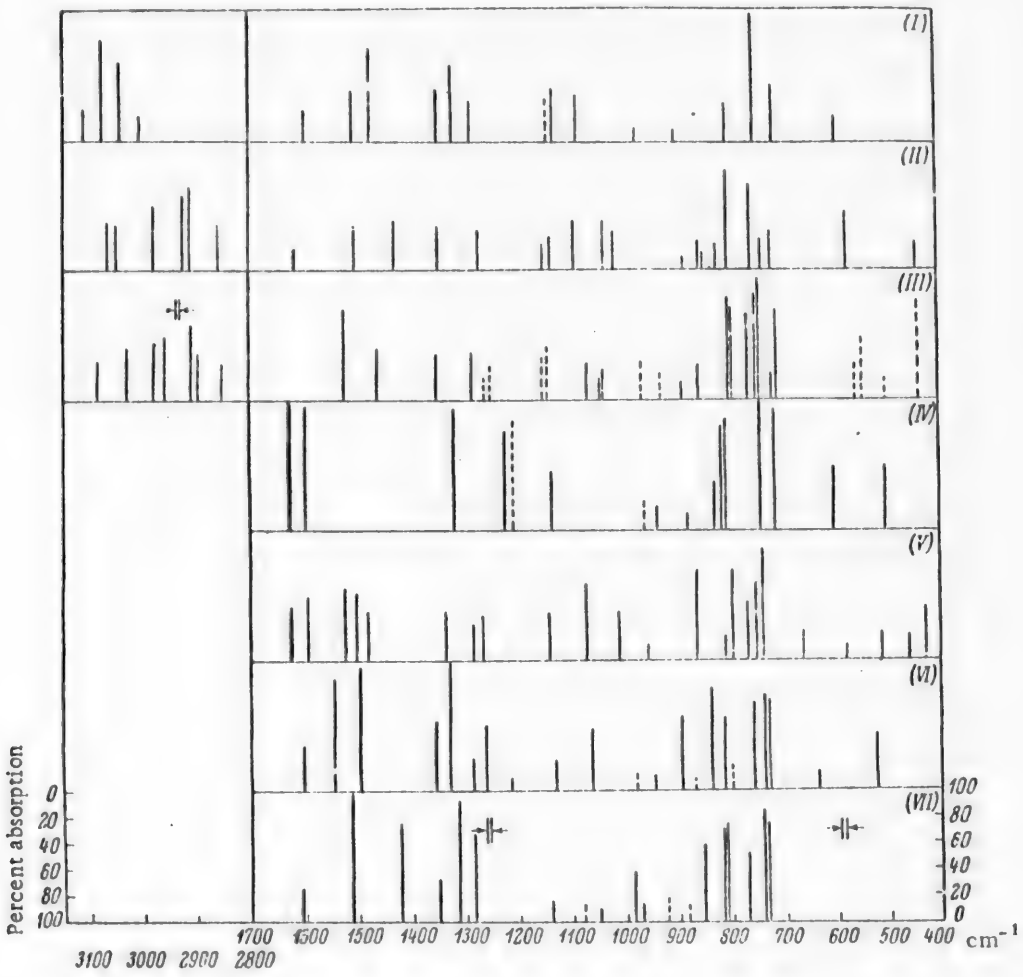
The compounds mentioned were synthesized according to the methods given in [3]. Compound (III) was prepared by us for the first time by mixing aqueous solutions of 6.12 g of 2,3-toluylenediamine* and 6.47 g of selenious acid; the brown precipitate that separated out was filtered off and dried at 90°; yield 9.85 g, m.p. 106-107.5°. The compound was purified by steam distillation (m.p. 109-109.5°). After crystallization from alcohol (white platelets) it melted at 110.6-111.2° (corr.); λ_{max} (in 95% alcohol) 330 mμ (ϵ $3.44 \cdot 10^4$).

Found %: N 14.09, 14.28. $C_7H_6N_2Se$. Calculated %: N 14.21.

The infrared absorption spectra were measured in the region 400-1700 and 2800-3150 cm^{-1} with an IKS-11 spectrometer, the amplifier-recording part of which was replaced by a previously described arrangement [6]. For

* Prepared by reduction of o-nitro-m-toluidine with zinc dust in alcoholic alkali similar to the synthesis of o-phenylenediamine [5].

the work in the ranges chosen, we used interchangeable prisms of KBr, NaCl, and LiF; the values for the spectral width of the slit were:• 10 cm^{-1} at 400-600 cm^{-1}, 6 cm^{-1} at 600-1300 cm^{-1}, 10 cm^{-1} at 1300-1700 cm^{-1}, and about 7 cm^{-1} at 2800-3150 cm^{-1}.



Infrared absorption spectra of piazselenole and its derivatives

The absorption spectra of the compounds in the solid state were measured for samples made into a paste with vaseline oil (V.O.). The latter was purified by the usual method for paraffins [7]; for our work we used the fraction boiling at 287-300° (10 mm). In those parts of the spectrum where V.O. absorbs strongly, the infrared absorption spectra were recorded for samples dissolved in carbon tetrachloride. For correct evaluation of the intensity and better resolution of the spectrum, we were obliged to record at different thicknesses of the layer of the absorbing sample.

In the figure the spectra of compounds (I-VII) are shown. The absorption bands are shown as straight lines, the heights of which are equal to the percent absorption (transmission), taking into account the dispersed radiation at high frequencies in the spectrometer. The latter usually was large for paste samples in V.O. The values of the measured frequencies (in cm^{-1}) were as follows:

• The spectral width of the slit was calculated by the formula generally accepted for infrared prism spectrophotometers [6].

(I) – (N* 0.0675, d 0.501 mm) 3110, 3075, 3042, 3004, 1473, 1356; (d 0.047 mm; 0.1442 g per 0.4 ml V.O.) 1598, 1508, 1319, 1287, 1139, 1128, 1032, 971, 896, 799, 745, 709, 588.

(II) – (N 0.0727; d 0.199 mm) 3066, 3049, 2979, 2924, 2910, 2957, 1430, 1348; (d 0.096 mm; 0.0836 g per 0.75 ml V.O.) 1616, 1504, 1272, 1149, 1140, 1089, 1033, 1014, 882, 853, 845, 821, 800, 754, 736, 718, 572, 439.

(III) – (N 0.0885; d 0.508 mm) 3085, 3030, 2980, 2960, 2910, 2896, 2852; (d 0.206 mm) 1463, 1351; (d 0.025 mm; 0.1088 g per 0.15 ml O.V.) 1526, 1286, 1067, 1042, 1037, 887, 856, 799, 795, 763, 749, 742, 718, 709; (d 0.047 mm) 1263, 1251, 1152, 1143, 964, 928, 557, 544, 500, 438.

(IV) – (d 0.019mm; 0.1010 g per 0.15 ml V.O.) 1628, 1598, 1319, 1225, 1136, 936, 827, 815, 807, 743, 715, 603, 502; (d 0.047 mm) 1209, 961, 878.

(V) – (d 0.019 mm; 0.0677 g per 0.1 ml V.O.) 1627, 1596, 1526, 1505, 1483, 1337, 1286, 1268, 1143, 1072, 1012, 957, 864, 811, 797, 769, 752, 739, 662, 580, 514, 461, 428.

(VI) – (d 0.019 mm; 0.060 g per 0.15 ml V.O.) 1604, 1546, 1498, 1356, 1330, 1287, 1263, 1216, 1131, 1064, 995, 946, 839, 815, 759, 738, 729, 636, 525; (d 0.047 mm) 980, 871, 800.

(VII) – (d 0.019 mm; 0.0930 g per 0.15 ml V.O.) 1609, 1515, 1423, 1315, 1286, 1141, 1051, 986, 971, 965, 865, 818, 812, 771, 741, 733; (d 0.047 mm) 1080, 924, 885.

The accuracy of the measurements of intensity of the absorption bands did not exceed 3% absolute. We therefore do not give here the values for the intensities, which can be obtained with the indicated degree of accuracy from the corresponding figures.

DISCUSSION OF RESULTS

Aromatic CH valence vibrations are known to appear at about 3038 cm^{-1} in the form of three absorption bands when a lithium fluoride prism is used. In the figure it can be seen that in this region absorption bands were observed at the following frequencies (cm^{-1}): 3110, 3075, 3042, 3004 (for I); 3066, 3049 (for II); 3085, 3030 (for III). In this instance (as for substituted benzenes) a decrease in the intensity and the number of absorption bands takes place when the number of substituents increases. In addition, we can notice an appreciable shift of the absorption bands in this region in comparison with the position of the absorption bands of substituted benzenes. Thus, in the spectra of the piazselenoles there are "aromatic"** CH valence vibrations. However, the fact that the position of the absorption bands is shifted certainly is connected with the disruption of the equivalence of the bonds in the benzene ring of the molecules of these compounds. It is pertinent to mention that o-benzoquinones also have "aromatic" absorption in this region with the same type of shift in position of the bands [8].

In the region of the absorption of the ordinary aromatic carbon-carbon bonds (1650-1475 cm^{-1}) we find the following frequencies (cm^{-1}): 1598, 1508, 1473 (for I); 1616, 1504 (for II); 1526 (for III); 1628, 1598 (for IV); 1627, 1596, 1505, 1483 (for V); 1604, 1546, 1498 (for VI); 1609, 1515 (for VII). o-Benzoquinones also have such "aromatic" absorption bands [8]. For o-benzoquinones and also for the piazselenoles it is difficult to find a relationship between the position of these absorption bands and the relative arrangement of the substituents. The similarity that is noticed in the IR spectra of the o-benzoquinones and the derivatives of piazselenole indicates the o-quinonimide structure of piazselenole. Apparently some of the frequencies listed above should be related to the –C = N valence vibrations in the same way as Boyer et al., relate to this the frequencies in the region 1616-1634 cm^{-1} in the spectrum of benzofuroxan [9].

Absorption frequencies of the aromatic ring usually are found also in the region 1250-1000 cm^{-1}, with the distribution of the bands depending on the relative position of the substituents. Such a relationship can be established also for the derivatives of (I), if we regard them as substituted benzenes and compound (I) as a 1,2-substituted benzene. Thus, it is possible to distinguish the following groups of absorption bands: 1,2-substitution (compound I) in the range 1139-1082 cm^{-1}; 1,2,4-substitution (compounds II, IV, VI) in the range 1225-1014 cm^{-1} (in contrast to the 1,2-type there are strong bands in the range 1225-1139 cm^{-1} and bands at 1082-1014 cm^{-1}); 1,2,3-substitution (compounds III, V, VII) in the region 1143-1012 cm^{-1}.

* N is the mole fraction of the compound in CCl_4 solution.

** We apply the name "aromatic" to those vibrations of the substituted benzene ring of the piazselenole molecule which fall in the region of the vibrations of the ordinary aromatic ring.

The exact position of the absorption bands corresponding to the deformed CH vibrations in the aromatic ring in the region 900-680 cm^{-1} depends on the number and position of the substituents. A similar relationship is characteristic also of the piazselenoles: 1,2-substitution (compound I) strong absorption at 745 cm^{-1}, weak absorption at 709 cm^{-1}, very weak at 800 cm^{-1}; 1,2,4-substitution (compounds II, IV, VI) strong absorption in the region 825-729 cm^{-1}, or rather at 825 and 745-729 cm^{-1}, weak absorption at 715 cm^{-1}. In contrast to the 1,2-type, this type of substitution is characterized by an absorption maximum in the region 825-810 cm^{-1}. 1,2,3-Substitution (compounds III, V, VII) differs from the 1,2,4-type in the strong absorption in the range 856-856 cm^{-1}.

If the rules derived are developed without taking into account the absorption of the nitropiazselenoles (VI, VII), the intervals derived as characteristic of the type of substitution turn out to be narrower. It is important to point out that it is also possible to derive for the "aromatic" deformations of the CH vibrations of the o-benzoquinones such type intervals, which are close to those just indicated for the piazselenoles.

The methyl group. The absorption bands with frequencies at 2979, 2924, 2910, and 2857 cm^{-1} (II) and at 2980, 2960, 2910, 2896 and 2852 cm^{-1} (III) certainly are related to the CH valence vibrations of the methyl group. For the o-benzoquinones they are located at about 2941-2857 cm^{-1} [8]. Thus, the position of these bands both in the piazselenole series and for the methyl derivatives of the o-benzoquinones is close to that for the case where the CH_3 group is linked with an aromatic carbon atom (it is well known that in this instance there are two intense characteristic bands at 2962 and 2872 cm^{-1}, corresponding to the symmetric and the antisymmetric vibrations). The bands at the frequencies 1430 cm^{-1} (II) and 1463 cm^{-1} (III), and at 1348 cm^{-1} (II) and 1351 cm^{-1} (III) are related respectively to the antisymmetric and the symmetric deformation vibrations of the methyl group.

The amino group. In primary aromatic amines the NH_2 group absorbs in the region 1590-1650 cm^{-1}, which, as a rule, coincides most frequently with the absorption interval of the aromatic ring; therefore a part of the bands previously related to the valence vibrations of the carbon-carbon bonds of the "aromatic" ring should be ascribed also to the vibrations of this group. The bands at 1598 cm^{-1} (IV) and 1596 cm^{-1} (V) can be related to the N-H deformation vibrations, as has been done for aminobenzoquinone [10]. The bands found at 900-650 cm^{-1} also, apparently, are related both to the CH deformation vibrations and to the deformation vibrations of the NH_2 group. The valence vibrations of the C-N bond for primary aromatic amines are found at 1340-1250 cm^{-1}. The corresponding vibrations of the aminopiazselenoles are located at 1268, 1286, and 1337 cm^{-1} (V) and 1319 cm^{-1} (IV). By analogy with [10], it is probable that the bands at 1225 cm^{-1} (IV) also are of the same nature.

The nitro group. The aromatic nitro compounds have bands at 1560-1500 cm^{-1} and 1360-1300 cm^{-1}, which correspond to the symmetric and antisymmetric valence vibrations of the NO_2 group. In the case of the nitropiazselenoles the absorption bands with a frequency of 1498 or 1546 cm^{-1} (VI) and at 1515 cm^{-1} (VII) might be related to the antisymmetric vibrations of the NO_2 group, since they are very intense. It is impossible to determine this definitely, however, because the frequencies referred to fall in the absorption interval already mentioned for carbon-carbon and azomethine bonds. The aromatic nitro group is characterized by frequencies at 760-720 cm^{-1}, which coincide with the region of the deformation vibrations of the ring. The NO_2 group may also have bands below 500 cm^{-1}, but this region was experimentally difficult for us to work in. The frequencies 1330 cm^{-1} (VI) and 1315 cm^{-1} (VII) are related to the symmetric vibrations of the NO_2 group. Continuing to regard piazselenole as a 1,2-substituted benzene, we may note that these frequencies of the nitropiazselenoles suggest the absorption of an aromatic nitrocompound having a strongly electronegative substituent in the para position. The latter agrees completely with the electronophilic nature of the condensed selenodiazole ring.

The selenodiazole ring is similar to the furazan [oxadiazole] and the furoxan rings with respect to both its electronophilic nature and its structure. Comparison shows that in the IR spectra of the furazans [11] the furoxans [12], and their benzologs [9, 13] there are repeated absorption bands which can be related to the vibrations of the oxadiazole ring. The absorption bands close to them in frequency (at 865-980, 946-995, 1030-1070, 1150, 1660-1630 cm^{-1}), which are also in the spectra of all the piazselenoles studied, can therefore be related to the absorption of the selenodiazole ring.

SUMMARY

1. The similarity of the infrared spectra of piazselenole and its derivatives to the infrared spectra of the o-benzoquinones has been shown; "aromatic" absorption bands are characteristic of both types of compounds.

2. The relationship of the distribution and the number of absorption bands for deformed C-H vibrations to the position of the substituent in the piazselenole molecule has been determined.

3. In the infrared spectra of the piazselenoles a number of absorption bands characteristic of heterocyclic vibrations have been recorded.

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•Original Russian pagination. See C. B. Translation.

THE ADDITION OF AROMATIC AMINES AND PHENYLHYDRAZINE TO 2-METHYL-5-VINYLPYRIDINE

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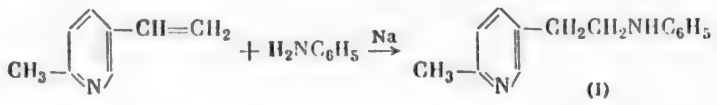
In recent years the production of vinylpyridines, which are used as copolymers with styrene and esters of acrylic acid, has been established in a number of countries. In connection with this a systematic study has been started of the properties of these materials, and in particular it has been found that α-vinylpyridine rather readily adds compounds having a labile hydrogen atom [1, 2].

We have investigated this type of reaction in the case of 2-methyl-5-vinylpyridine. This compound at the present time is produced on a commercial scale by the dehydrogenation of 2-methyl-5-ethylpyridine and is the most readily available representative of the β-vinylpyridines, which have been little investigated. There are data in the literature indicating that this vinylpyridine in the presence of metallic sodium adds aniline, methylaniline, and morpholine, but under the same conditions it does not react with cyclohexylamine, dibutylamine, pyrrole, and piperidine [3].

We carried out the reaction of 2-methyl-5-vinylpyridine with 2 moles of aromatic amine by heating for 4-5 hours on a water bath in the presence of 0.1 g-atom of metallic sodium. In this way we obtained 2-methyl-5-(2-phenylaminoethyl)pyridine (I) in 71.5% yield from aniline, as shown in the following scheme:



(I)

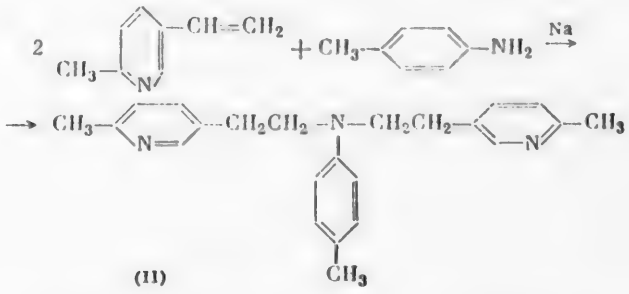
The aniline group proved to be in the β-position of the side chain in this product, similar to what takes place, for example, when aniline adds to acrylonitrile. The 2-methyl-5-(2-phenylaminoethyl)pyridine obtained in this case differed in its properties from the 2-methyl-5-(1-phenylaminoethyl)pyridine synthesized from 2-methyl-5-(1-bromoethyl)-pyridine and aniline [4].

Like aniline, such compounds as ethylaniline, o-, m-, and p-toluidine, o- and p-anisidine add to 2-methyl-5-vinylpyridine. In this process the para-substituted compounds react more readily than the meta or ortho isomers. When the reaction was carried out with β-naphthylamine, a low yield (21.5%) of addition product was obtained, which is explained to a considerable extent by the difficulties of isolation. In the case of p-phenylenediamine the reaction was complicated by oxidation processes, and we did not succeed in isolating the reaction product.

When the basicity of the amino group was lowered, the ability to add decreased. Thus, diphenylamine, o-nitroaniline, indole, acetamide, and phthalimide did not react with our β-vinylpyridine under the conditions described for the reaction of these (or similar) compounds with α-vinylpyridine. In these instances we invariably recovered the starting materials or, in some cases, observed the violent polymerization of 2-methyl-5-vinylpyridine.

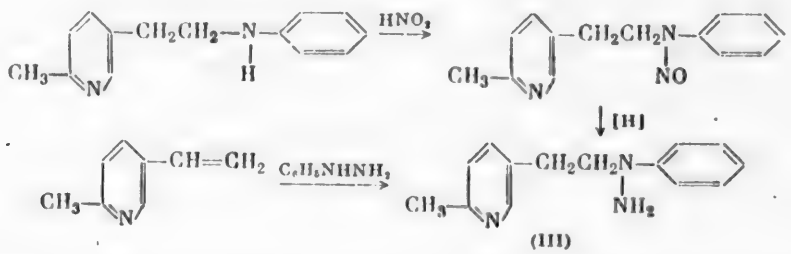
Our attempts to carry out a reaction with acetoacetic ester, ethyl or butyl alcohol, phenol, and sodium bisulfite were likewise unsuccessful. This confirms that the β-vinylpyridines add such compounds with more difficulty than the α-isomers.

In the case of p-toluidine, in the molecule of which the amino group is more basic as a result of the inductive effect of the methyl group, we observed the formation of a high-boiling by-product of the reaction. This substance was produced more easily with an equimolar ratio of the reactants and corresponded in composition to the addition product of 2 molecules of 2-methyl-5-vinylpyridine and 1 molecule of the amine – N,N-bis[2-(2-methylpyridyl-5)-ethyl]-p-toluidine (II).



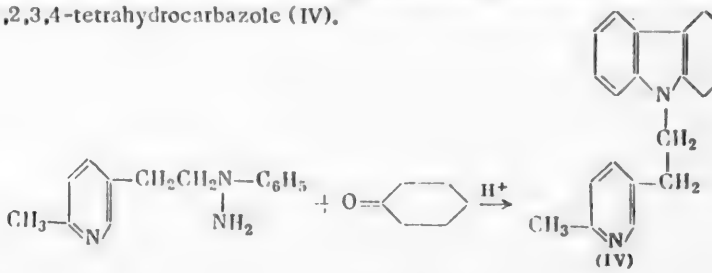
(II)

The structure of this compound was confirmed by the fact that in its infrared spectrum the absorption band in the region 3000-3500 cm^{-1} characteristic of the N-H bond was absent, while in the products of the addition of 1 mole of 2-methyl-5-vinylpyridine to primary aromatic amines of this type an intense band is found in all cases. Furthermore, compounds of the type of (I) are easily nitrosated as a result of the presence of the NH group, while compound (II) is not capable of such reactions. In particular, compounds of type (I) are rather easily nitrosated, with the formation of N-nitroso compounds. The position of the nitroso group is verified, first, by the fact that under these conditions neither α-picoline nor 2-methyl-5-ethylpyridine is nitrosated (this was checked in special experiments), second, by the capacity of N-nitroso compounds of such a type to rearrange into a benzene ring, and finally, by the reduction of the N-nitroso compound to the N-amino compound (III). The latter can also be obtained, it appeared, by direct reaction of 2-methyl-5-vinylpyridine with phenylhydrazine. The above-described chain of transformations shows, at the same time, that this addition takes place as a result of the amino group which is directly connected to the phenyl group.



(III)

Compound (III) was a typical arylhydrazine. For example, when it was reacted with cyclohexanone and subsequently treated with sulfuric acid, a Fisher rearrangement took place, with the formation of N-[2-(2-methylpyridyl-5)-ethyl]-1,2,3,4-tetrahydrocarbazole (IV).



(IV)

Most of the compounds synthesized had the consistency of very thick oils under ordinary conditions. This also was true of the acyl derivatives. The hydrochlorides both of the bases themselves and of the acyl derivatives (formed as a result of the pyridine nitrogen atom) were rather hygroscopic.

Preliminary tests carried out in the department of pharmacology of the Minsk Medical Institute showed that on intraperitoneal injection into mice, solutions of the hydrochlorides of the compounds prepared had the property of stimulating the parasympathetic nervous system (muscarine and nicotine effect). The toxicity (LD_{100}) of most of the preparations varied within the limits 300-500 mg/kg of weight. Acylation of the amino group led to an increase in toxicity of the preparation. The presence of a nitroso group in the para position of the aromatic ring increased the toxicity of the preparation 5 times. As would be expected, the methiodides proved to be more toxic than the corresponding hydrochlorides. The pharmacological investigation of the compounds prepared is being continued.

EXPERIMENTAL

2-Methyl-5-(2-phenylaminoethyl)pyridine (I). (a) A mixture of 98 g of aniline, 75 g of 2-methyl-5-vinylpyridine, and 2.3 g of metallic sodium was heated for 5 hours on a boiling water bath, with stirring. Five ml of alcohol was added and the unreacted starting materials were steam-distilled off. The crystals that precipitated after cooling were separated, dried, and purified by vacuum distillation. Yield 94.5 g (71.5%), b.p. 194-195° (5 mm), m.p. 76-77° (from 70% aqueous alcohol). Literature data [3]: b.p. 192-194° (6 mm).

Found %: C 79.24; 79.42; H 7.52; 7.52; N 13.17, 13.19. $C_{14}H_{16}N_2$. Calculated %: 79.24; H 7.60; N 13.20.

Dihydrochloride, m.p. 160-162° (from alcohol).

Found %: HCl 25.00, 25.08. $C_{14}H_{18}N_2Cl_2$. Calculated %: HCl 24.76.

Methiodide, m.p. 154-155° (from alcohol).

Found %: I 35.75, 35.65. $C_{15}H_{19}N_2I$. Calculated %: I 35.83.

There was an intense absorption band at 3256 cm^{-1} in the infrared spectrum.

2-Methyl-5-(N-formyl-2-phenylaminoethyl)pyridine was obtained by heating 8.48 g of (I) with 6.5 ml of formic acid. B.p. 201° (5 mm), thick oil.

Methiodide, m.p. 166° (from alcohol).

Found %: I 33.12, 32.99. $C_{16}H_{19}ON_2I$. Calculated %: I 33.20.

2-Methyl-5-(N-acetyl-2-phenylaminoethyl)pyridine was obtained by heating 4.24 g of (I) with 5 ml of acetic anhydride, b.p. 202-203° (2.5 mm), thick oil.

Found %: N 11.00, 11.13. $C_{16}H_{18}ON_2$. Calculated %: N 11.02.

Methiodide, m.p. 158-159°.

Found %: I 31.62, 31.64. $C_{17}H_{21}ON_2I$. Calculated %: I 32.03.

2-Methyl-5-(N-benzoyl-2-phenylaminoethyl)pyridine was obtained by benzoylation of (I) by the Schotten-Baumann method. M.p. 86-87° (from aqueous alcohol).

Found %: C 80.14, 80.17; H 6.42, 6.43; N 8.59, 8.81. $C_{21}H_{20}ON_2$. Calculated %: C 79.74; H 6.33; N 9.06.

Absorption in the 3000-3500 cm^{-1} region was absent in the IR spectrum.

2-Methyl-5-(N-nitroso-2-phenylaminoethyl)pyridine formed light-yellow crystals; they were recrystallized from a mixture of petroleum ether and benzene (9:1), m.p. 63-64°.

Absorption in the 3000-3500 cm^{-1} region was absent in the IR spectrum.

2-Methyl-5-(2-o-tolylaminoethyl)pyridine (V) was obtained in a manner similar to (I) from 64.2 g of o-toluidine, 35.7 g of 2-methyl-5-vinylpyridine, and 1.38 g of metallic sodium. The reaction time was 3 hours. Yield 46.3 g (68.2%), b.p. 199-201° (3 mm), m.p. 75-76° (from 70% alcohol).

Found %: C 79.68, 79.92; H 8.26, 8.23; N 12.56, 12.54. $C_{15}H_{18}N_2$. Calculated %: C 79.60; H 8.02; N 12.38.

There was an intense absorption band at 3312 cm^{-1} in the IR spectrum.

Monomethiodide, m.p. 193-194° (from alcohol).

Found %: I 34.41, 34.19. $C_{16}H_{21}N_2I$. Calculated %: I 34.47.

2-Methyl-5-(N-acetyl-2-o-tolylaminoethyl)pyridine was obtained by the acetylation of 2-methyl-5-(2-o-tolylaminoethyl)pyridine (IV) with acetic anhydride, b.p. 205° (2 mm).

Found %: N 10.12, 1033. $C_{17}H_{20}ON_2$. Calculated %: N 10.44.

2-Methyl-5-(2-m-tolylaminoethyl)pyridine was obtained in a manner similar to the preceding preparation from 64.2 g m-toluidine, 35.7 g of 2-methyl-5-vinylpyridine, and 1.38 g of metallic sodium. Yield 44.7 g (66.0%), b.p. 198-200° (3 mm), m.p. 54.5-55° (from alcohol).

Found %: C 79.65, 79.70; H 8.16, 8.17; N 12.51, 12.52. $C_{15}H_{18}N_2$. Calculated %: C 79.60; H 8.02, N 12.38.

There was an intense absorption band at 3314 cm^{-1} in the IR spectrum.

Dihydrochloride, m.p. 175-176° (from anhydrous alcohol).

Found %: HCl 24.64, 24.81. $C_{15}H_{20}N_2Cl_2$. Calculated %: HCl 24.36.

Monomethiodide, m.p. 151-152° (from alcohol).

Found %: I 34.11, 34.07. $C_{16}H_{21}N_2I$. Calculated %: I 34.47.

2-Methyl-5-(N-acetyl-2-m-tolylaminoethyl)pyridine was obtained by the acetylation of 2-methyl-5-(2-m-tolylaminoethyl)pyridine (VI) with acetic anhydride, b.p. 212-214° (6 mm).

Found %: N 10.43, 10.52. $C_{17}H_{20}ON_2$. Calculated %: N 10.44.

Methiodide, m.p. 154-155° (from alcohol).

Found %: I 30.84, 30.62. $C_{18}H_{23}ON_2I$. Calculated %: I 30.93.

2-Methyl-5-(2-p-tolylaminoethyl)pyridine (VII) was synthesized in a manner similar to 2-methyl-5-(2-o-tolylaminoethyl)pyridine from 64.2 g of p-toluidine, 35.7 g of 2-methyl-5-vinylpyridine, and 1.38 g of metallic sodium. Yield 52.17 g (77.2%), b.p. 191-193° (3 mm), m.p. 65-66° (from aqueous alcohol).

Found %: C 79.72, 79.82; H 8.10, 8.12; N 12.27, 12.32. $C_{15}H_{18}N_2$. Calculated %: C 79.60; H 8.02; N 12.38.

Dihydrochloride, m.p. 187-189° (from alcohol).

Found %: HCl 24.37, 24.59. $C_{15}H_{20}N_2Cl_2$. Calculated %: HCl 24.36.

In a similar experiment using 128.48 g of p-toludine, 143.5 g of 2-methyl-5-vinylpyridine, and 2.76 g of metallic sodium, we obtained 192 g (70%) of 2-methyl-5-(2-p-tolylaminoethyl)pyridine and 10.0 g of N,N-bis[2-(2-methylpyridyl-5)-ethyl]-p-toluidine (II) with b.p. 235-237° (2 mm), m.p. 90-91°.

Found %: C 80.13, 80.01; H 8.22, 8.24; N 12.29, 12.11. $C_{23}H_{27}N_3$. Calculated %: C 79.96; H 7.88; N 12.16.

Absorption in the region 3000-3500 cm^{-1} was absent in the IR spectrum.

2-Methyl-5-(N-acetyl-2-p-tolylaminoethyl)pyridine was obtained by the acetylation of 2-methyl-5-(2-p-tolylaminoethyl)pyridine (VII) with acetic anhydride, b.p. 190-195° (2 mm).

Hydrochloride, m.p. 151-152° (from anhydrous alcohol).

Found %: HCl 11.95, 12.05. $C_{17}H_{21}ON_2Cl$. Calculated %: HCl 11.96.

Methiodide, m.p. 185° (from alcohol).

Found %: I 30.54, 30.48. $C_{18}H_{23}ON_2I$. Calculated %: I 30.93.

2-Methyl-5-(2-o-anisylaminoethyl)pyridine (VIII) was obtained in a manner similar to 2-methyl-5-(2-o-tolylaminoethyl)pyridine (V) from 49.2 g of o-anisidine, 23.8 g of 2-methyl-5-vinylpyridine, and 0.9 g of metallic sodium. Yield 11.7 g (24.4%), b.p. 201-203° (4 mm). Thick liquid.

Dihydrochloride, m.p. 168-170° (from alcohol).

Found %: HCl 21.6, 21.5. $C_{15}H_{20}ON_2Cl_2$. Calculated %: HCl 21.0.

2-Methyl-5-(N-acetyl-2-o-anisylaminoethyl)pyridine was obtained by the acetylation of 2-methyl-5-(2-o-anisylaminoethyl)pyridine (XIII) with acetic anhydride, b.p. 220-222° (3 mm).

Methiodide, m.p. 172-173° (from alcohol).

Found %: I 29.63, 29.70. $C_{18}H_{23}O_2N_2I$. Calculated %: I 29.77.

2-Methyl-5-(2-p-anisylaminoethyl)pyridine (IX) was obtained in a manner similar to 2-methyl-5-(2-o-tolylaminoethyl)pyridine (V) from 49.2 g of p-anisidine, 23.8 g of 2-methyl-5-vinylpyridine, and 0.9 g of metallic sodium. Yield 31.3 g (65.0%), b.p. 209-212° (4 mm). Thick liquid.

Dimethiodide, m.p. 240° (from alcohol).

Found %: C 38.63, 38.67; H 5.12, 5.12. $C_{17}H_{24}ON_2I_2$. Calculated %: C 38.80; H 4.62.

2-Methyl-5-(N-acetyl-2-p-anisylaminoethyl)pyridine was obtained by the acetylation of 2-methyl-5-(2-p-anisylaminoethyl)pyridine (IX), b.p. 232° (3 mm).

Methiodide, m.p. 163° (from anhydrous alcohol).

Found %: I 29.45, 29.64 $C_{18}H_{23}O_2N_2I$. Calculated %: I 29.77.

2-Methyl-5-(N-ethyl-2-phenylaminoethyl)pyridine. A mixture of 48.4 g of ethylaniline, 23.8 g of 2-methyl-5-vinylpyridine, and 1.0 g of metallic sodium was heated for 5 hours, with stirring, on a boiling water bath, the unreacted starting materials were steam-distilled off, the residue was extracted with ether, dried, the ether distilled off, and the residue was distilled in vacuum. Yield 22.5 g (47%) of 2-methyl-5-(N-ethyl-2-phenylaminoethyl)-pyridine (X) in the form of a thick yellow oil with b.p. 195-200° (7 mm) (the absorption band in the region 3000-3500 cm^{-1} was absent in the IR spectrum) and 3.5 g of a material with b.p. 280-290° (7 mm), which was not further investigated.

Monopicrate, m.p. 167-168° (from alcohol).

Found %: C 56.36, 56.46; H 5.05, 5.11; N 14.42, 14.45. $C_{22}H_{23}O_7N_5$. Calculated %: C 56.30; H 4.94; N 14.92.

Dihydrochloride, m.p. 170-172° (from alcohol).

Found %: HCl 23.76, 23.83. $C_{16}H_{22}N_2Cl_2$. Calculated %: HCl 23.28.

2-Methyl-5-[2-(N-p-nitrosophenyl-N-ethylamino)ethyl]pyridine was obtained by the nitrosation of the preceding compound (X). Bright-green crystals after recrystallization from a mixture of petroleum ether and benzene melted at 83-84°.

Found %: C 71.64, 71.88; H 7.25, 7.11; N 15.04, 14.91. $C_{16}H_{19}ON_3$. Calculated %: C 71.34; H 7.11; N 15.60.

Dihydrochloride, m.p. 173-175° (decomp., from alcohol).

Found %: HCl 21.39, 21.61. $C_{16}H_{21}ON_3Cl_2$. Calculated %: HCl 21.31.

2-Methyl-5-(2-β-naphthylaminoethyl)pyridine was obtained in a manner similar to 2-methyl-5-(2-o-tolylaminoethyl)pyridine (V) from 31.47 g of β-naphthylamine, 23.8 g of 2-methyl-5-vinylpyridine, and 1.0 g of metallic sodium. Yield 12.5 g (21.5%), b.p. 320° (2 mm), m.p. 110-111° (from benzene).

Found %: C 82.44, 82.12; H 7.11, 7.18; N 10.67, 10.52. $C_{18}H_{18}N_2$. Calculated %: C 82.40; H 6.92; N 10.68.

There was an intense absorption band at 3250 cm^{-1} in the IR spectrum.

2-Methyl-5-(N-amino-2-phenylaminoethyl)pyridine (III). (a) To a solution of 48.2 g of N-nitroso derivative of compound (I) mixed with 250 ml of acetic acid and 80 ml of water at a temperature from -3 to -5° there was added in small portions, with stirring, 120 g of zinc dust. When the addition was ended, the mixture was stirred for 1 hour longer, the excess zinc was filtered off, 40% sodium hydroxide solution was added until all the zinc hydroxide dissolved, the mixture was extracted with ether, the extract was dried, the ether distilled off, and the residue was distilled in vacuum in a current of nitrogen. Yield of compound (III) 38.0 g (83.6%), b.p. 180° (2 mm).

Dipicrate, m.p. 158-159° (decomp., from alcohol).

(b) Five-tenths gram of metallic sodium was dissolved in 22.4 g of phenylhydrazine by heating on a boiling water bath, and to this solution was added dropwise 23.8 g of 2-methyl-5-vinylpyridine. The mixture was heated for 6 hours longer, 5 ml of alcohol was added, the mixture was poured into water, extracted with ether, the extract was dried, the ether was distilled off, and the residue was distilled in vacuum. Yield 35.9 g (79%).

Dipicrate, 158-159° (from alcohol).

Found %: C 45.95, 46.08; H 3.46, 3.53. $C_{26}H_{23}O_{14}N_9$. Calculated %: C 45.55; H 3.38.

A mixed sample with the dipicrate obtained by method (a) gave no depression in melting point.

Dihydrochloride, m.p. 196-198° (from anhydrous alcohol).

Found %: HCl 24.39, 24.52. $C_{14}H_{19}N_3Cl_2$. Calculated %: HCl 24.29.

N-[2-(2-Methylpyridyl-5)-ethyl]-1,2,3,4-tetrahydrocarbazole (IV). Five and five-tenths grams of compound (III) and 2 g of cyclohexanone were boiled on netting for 0.5 hour. Fifty ml of hot 20% sulfuric acid was added to the hot mixture, which foamed up. After boiling for 10 minutes, the solution was cooled and the sulfate of the carbazole (IV) was separated. Yield 5.0 g (70%) with m.p. 174-175° (from water). After neutralization with sodium carbonate, the free carbazole (IV) was obtained with m.p. 72-73° (from petroleum ether).

Found %: C 82.76, 82.51; H 7.88, 7.69. $C_{20}H_{22}N_2$. Calculated %: C 82.72; H 7.64.

SUMMARY

1. It has been shown that 2-methyl-5-vinylpyridine when heated in the presence of metallic sodium adds aromatic amines, and the aryl amino group proved to be in the β-position of the side chain. When the basicity of the amine decreased, the reaction did not go under these conditions.

2. 2-Methyl-5-vinylpyridine was considerably weaker than 2-vinylpyridine in its capacity for addition reactions.

3. 2-Methyl-5-vinylpyridine adds phenylhydrazine (as a result of the imino group), and the hydrazine formed can be used in the Fischer synthesis.

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CONDENSATION OF ALDEHYDES AND KETONES

VII. CONDENSATION OF CYCLOHEXANONE WITH 1,3-DI-(p-DIMETHYLAMINOBENZAL)CYCLOHEXANONE-2

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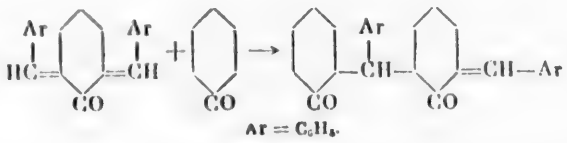
It has been shown recently [1] that dibenzalcyclohexanone condenses readily under the influence of sodium hydroxide in an alcoholic solution with one molecule of cyclohexanone by the scheme



Ar = C_6H_5.

In order to extend this reaction to substituted dibenzalcyclohexanones we studied the condensation of cyclohexanone with 1,3-di-(p-dimethylaminobenzal)cyclohexanone-2.

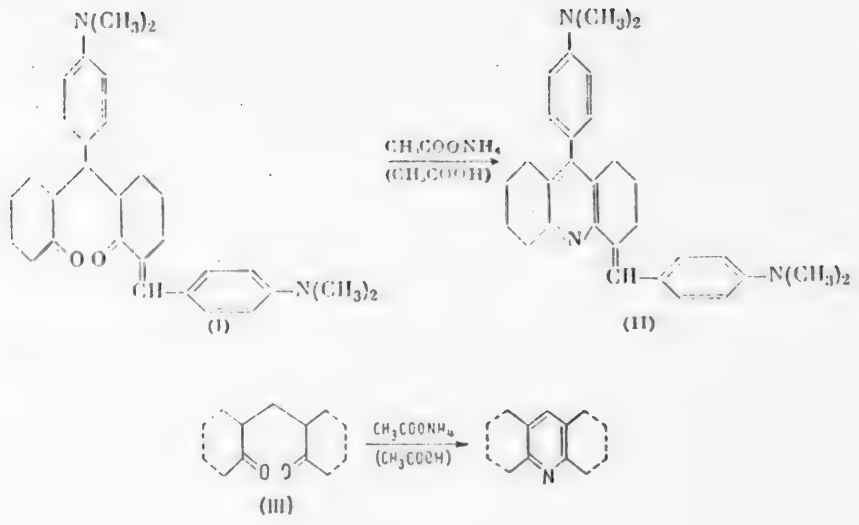
In view of the exceptional difficulty of dissolving this diarylidenecyclohexanone in alcohol, we attempted to carry out the reaction in pyridine, chloroform, dioxane, and, finally, in cyclohexanone. The reaction did not go in pyridine and cyclohexanone under the influence of diethylamine. Reaction also did not take place under the influence of sodium acetate in chloroform and dioxane. In cyclohexanone under the influence of 10% alcoholic sodium hydroxide solution the reaction proceeded according to the diagram [Ar = p-$C_6H_4N(CH_3)_2$] rather easily, and p-dimethylaminobenzylidene-p-dimethylaminobenzaldicyclohexanone (I) was produced in good yield.

The structure of compound (I) was confirmed by its reactions. The compound formed the corresponding hydrazone with two molecules of 2,4-dinitrophenylhydrazine, and under the conditions of the improved pyridine synthesis of Chichibabin [2] it gave a base of the expected formula $C_{30}H_{35}N_3$. The first reaction confirmed the presence in the compound of two carbonyl groups. The second reaction showed that these two groups were in the 1,5 position relative to each other in the carbon chain, which is favorable to the formation of a pyridine ring. All of this corresponds completely with formula (I).

Under the conditions of the pyridine synthesis it was possible to produce from the 1,5-diketone (I) only the hydroacridine base (II), 4-(p-dimethylaminobenzylidene)-9-(p-dimethylaminophenyl)octahydroacridine.

This follows both from the reactions of the base obtained, and also from the literature data [3] on the course of this synthesis with 1,5-diketones of the type of (III), to which the diketone (I) belongs.

In the case of bicyclohexanones the symmetrical octahydroacridines are formed [3].



EXPERIMENTAL*

p-Dimethylaminobenzylidene-p-dimethylaminobenzaldicyclohexanone. To a boiling solution of 17 g of di(p-dimethylaminobenzal)cyclohexanone in 180 ml of cyclohexanone was carefully added through the reflux condenser 35 ml of 10% alcoholic sodium hydroxide solution. The solution was boiled for 5 minutes and then cooled by keeping the flask with the reaction mixture in a freezing mixture for 3 hours. The crystals of the diketone (I) which precipitated were filtered out and washed with alcohol, then with water. Yield 17 g (78.7%), m.p. 225-227° (from dioxane). Long white needles, difficultly soluble in many of the usual organic solvents.

Found %: C 78.00, 78.31; H 8.30, 8.35; N 6.28, 6.41. $C_{30}H_{38}O_2N_2$. Calculated %: C 78.56; H 8.30; N 6.11.

The 2,4-dinitrophenylhydrazone was produced by mixing a hot alcoholic solution of the diketone with an alcoholic solution of 2,4-dinitrophenylhydrazine sulfate. Bright-orange rods, m.p. 184-186° (from a mixture of benzene and acetone 1:1).

Found %: N 17.50, 17.39. $C_{42}H_{46}O_8N_{10}$. Calculated %: N 17.11.

4-(p-Dimethylaminobenzylidene)-9-(p-dimethylaminophenyl)octahydroacridine. Fourteen grams of the diketone (I), 42 g of ammonium acetate, and 50 ml of glacial acetic acid were heated for 30 minutes with slight effervescence of the mixture. The light-orange solution that was formed was cooled and neutralized with 20% sodium carbonate solution. The precipitate that separated was filtered off and washed with water. Yield 13.1 g (98%). M.p. 236-238° (from alcohol). White prismatic rods, dissolving readily in alcohol, benzene, and acetone; difficultly soluble in ether and insoluble in water.

Found %: N 9.77, 9.85. $C_{30}H_{35}N_3$. Calculated %: N 9.61.

Picrate. When hot alcoholic solutions of the base and of picric acid were mixed, a light-brown oil immediately separated out, which completely solidified under water on the second day. Yellow rods (from dioxane), m.p. 242-243° (decomp.).

Found %: N 12.49, 12.40. $C_{36}H_{38}O_7N_6$. Calculated %: N 12.61.

The trihydrochloride was prepared by passing dry hydrogen chloride into a benzene solution of the base. From 2.5 g of the base, 2.9 g (93.5%) of the salt was obtained. M.p. 201-203° (from acetone). Colorless long rods, readily soluble in water, alcohol, and chloroform, difficultly soluble in acetone and dioxane, insoluble in benzene and ether.

Found %: Cl 19.08, 19.34. $C_{30}H_{35}N_3 \cdot 3HCl$. Calculated %: Cl 19.49.

* With the participation of student T. E. Emel'yanova.

SUMMARY

1. Cyclohexanone has been condensed with 1,3-di(p-dimethylaminobenzal)cyclohexanone-2.

2. It has been established that in this reaction only one molecule of cyclohexanone is added, and in this process an alicyclic 1,5-diketone is formed– p-dimethylaminobenzylidene-p-dimethylaminobenzaldicyclohexanone.

3. By the pyridine synthesis, the hydroacridine base 4-(p-dimethylaminobenzylidene)-9-(p-dimethylaminophenyl)octahydroacridine was prepared from the 1,5-diketone.

The compounds prepared have not been described in the literature.

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PHOTOREACTIONS OF ORGANOMETALLIC COMPOUNDS OF MERCURY IN SOLUTIONS

XV. PHOTOREACTIONS OF MERCURY-BIS-p-BENZOIC ACID AND ITS DIMETHYL ESTER*

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The photoreactions of the full phenyl compounds of mercury containing the functional groups methoxy and chlorine in the p-position with organic solvents were described in previous communications [1, 2].

In this paper we investigated the photoreactions of two organomercury compounds having carbomethoxy and carboxy groups in the p-position of the benzene rings found in diphenylmercury. As solvents we used methanol, dioxane, carbon tetrachloride and chloroform.

In methanol and dioxane the reaction went with the formation of mercury, benzoic acid (with mercury-bis-p-benzoic acid) or methyl benzoate (with the dimethyl ester of mercury-bis-p-benzoic acid), and formaldehyde (in methanol).

$$(p\text{-}RC_6H_4)_2Hg + CH_3OH \xrightarrow{h\nu} 2C_6H_5R + Hg + CH_2O$$
$$R = COOH,\ COOCH_3.$$

With carbon tetrachloride the dimethyl ester of mercury-bis-p-benzoic acid gives p-carbomethoxyphenylmercury chloride, mercurous chloride (traces), methyl ester of p-chlorobenzoic acid and hexachloroethane. As a result, the p-carbomethoxyphenyl radical reacts with CCl_4 in the same manner as do the phenyl and tolyl radicals [3] (with the cleavage of chlorine from the solvent) and differently from the p-methoxyphenyl radical [1].

p-Carbomethoxyphenylmercury chloride, mercurous chloride, mercury, methyl benzoate and hexachloroethane were obtained as the result of the photoreaction of dimethyl mercury-bis-p-benzoate with chloroform. The presence of p-carbomethoxyphenylmercury chloride (in CCl_4 and $CHCl_3$ media) indicates the gradual cleavage of p-carbomethoxyphenyl radicals from the dimethyl ester of mercury-bis-p-benzoic acid.

$$\left(p\text{-}CH_3OCC_6H_4\right)_2Hg \xrightarrow{h\nu} p\text{-}CH_3OCC_6H_4Hg\cdot + p\text{-}CH_3OCC_6H_4\cdot$$

Mercury-bis-p-benzoic acid failed to react witheither carbon tetrachloride or chloroform when irradiated for 150 hr.

* Communication XIV, Zhur. Obshchei Khim. 24, 260 (1954).

EXPERIMENTAL

Method of Operation. p-Carbomethoxyphenylmercury chloride, dimethyl mercury-bis-p-benzoate and mercury-bis-p-benzoic acid were prepared by the procedure of A. N. Nesmeyanov and L. G. Makarova [4]. The photoreactions were run in narrow (d 8 mm), thin-walled quartz test tubes, which were fastened 20 cm away from a PRK-4 quartz mercury-vapor lamp at a 30° angle from the horizontal. Irradiation was at room temperature.

1. Photoreaction of the dimethyl ester of mercury-bis-p-benzoic acid in methanol. A mixture of 0.15 g of dimethyl mercury-bis-p-benzoate and 12 ml of methanol was irradiated for 45 hr. The amount of metallic mercury that separated during this time was 0.056 g (87.5%). The filtrate remaining after removal of the mercury was distilled. Formaldehyde was found in the distillate. The dimedon derivative had m.p. 186°. The mixed melting point with the dimedon derivative of pure formaldehyde was not depressed. The residue from the distillation was saponified with 25% alcoholic caustic solution, and after the usual workup we obtained benzoic acid with m.p. 119°. The mixed melting point with pure benzoic acid was 119°.

2. Photoreaction of the dimethyl ester of mercury-bis-p-benzoic acid in dioxane. A mixture of 0.4 g of dimethyl mercury-bis-p-benzoate and 30 ml of dioxane (in two test tubes) was irradiated for 15 hr. We collected 0.16 g (94%) of metallic mercury. The filtrate was distilled. The residue from the distillation contained methyl benzoate (nD^{15} 1.5168). When saponified it gave benzoic acid with m.p. 120°. The mixed melting point with pure benzoic acid was not depressed.

3. Photoreaction of the dimethyl ester of mercury-bis-p-benzoic acid in carbon tetrachloride. A mixture of 0.6 g of dimethyl mercury-bis-p-benzoate and 45 ml of carbon tetrachloride was irradiated for 164 hr (three test tubes). The filtered precipitate was a mixture composed of 0.05 g (8%) of dimethyl mercury-bis-p-benzoate and 0.24 g (51%) of p-carbomethoxyphenylmercury chloride (the ratio was determined from the chlorine content in the mixture), the latter with m.p. 258-259° (from acetone). The mixed melting point with authentic p-carbomethoxyphenylmercury chloride was not depressed. Traces of mercurous chloride were obtained in some of the experiments.

From the distillation of the filtrate we isolated hexachloroethane with m.p. 183-184°. The residue from the distillation of the solvent was saponified with 5% alcoholic caustic solution. Acidification with hydrochloric acid gave p-chlorobenzoic acid with m.p. 235° (from aqueous dioxane). The mixture of this material with authentic p-chlorobenzoic acid also melted at 235°.

4. Photoreaction of the dimethyl ester of mercury-bis-p-benzoic acid in chloroform. A mixture of 0.5 g of dimethyl mercury-bis-p-benzoate and 12 ml of chloroform was irradiated for 54 hr. The precipitate was filtered. The precipitate was extracted with hot benzene to remove the organic portion. We obtained 0.02 g (9.4%) of mercury and 0.02 g (8%) of mercurous chloride. The portion soluble in benzene was a mixture of 0.14 g (28%) of unreacted dimethyl ester of mercury-bis-p-benzoic acid and 0.12 g (30.4%) of p-carbomethoxyphenylmercury chloride, the latter with m.p. 258° (from benzene).

The filtrate was distilled. Here we isolated hexachloroethane. The residue from the distillation was saponified to give benzoic acid with m.p. 119° (mixed melting point the same).

5. Photoreaction of mercury-bis-p-benzoic acid in methanol. A mixture of 0.2 g of mercury-bis-p-benzoic acid and 12 ml of methanol was irradiated for 270 hr. The filtered precipitate was a mixture composed of 0.07 g (77%) of metallic mercury and 0.03 g (15%) of unreacted mercury-bis-p-benzoic acid. The filtrate was shown to contain formaldehyde. The dimedon derivative had m.p. 185-186°. Another portion of the filtrate was worked up to give benzoic acid with m.p. 118°.

6. Photoreaction of mercury-bis-p-benzoic acid in dioxane. A mixture of 0.2 g of mercury-bis-p-benzoic acid and 15 ml of dioxane was irradiated for 95 hr. At the end of reaction we collected 0.085 g (93.7%) of mercury by filtration. The filtrate was treated with cold water. Here we obtained a small amount of benzoic acid with m.p. 119-120° (the mixed melting point was the same).

SUMMARY

1. Mercury, benzoic acid or methyl benzoate, and formaldehyde (in methanol) are formed in the photoreaction of mercury-bis-p-benzoic acid and dimethyl mercury-bis-p-benzoate in methanol and dioxane.

2. The photoreaction of dimethyl mercury-bis-p-benzoate in carbon tetrachloride yields p-carbomethoxyphenylmercury chloride, mercurous chloride, methyl p-chlorobenzoate and hexachloroethane. Running the photoreaction in chloroform yields p-carbomethoxyphenylmercury chloride, mercurous chloride, mercury, methyl benzoate and hexachloroethane.

3. Mercury-bis-p-benzoic acid does not react with either chloroform or carbon tetrachloride when irradiated

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PHOTOREACTION OF MERCURIC n-BUTYRATE

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Earlier [1] we had shown that the ultraviolet irradiation of mercuric acetate and mercuric propionate in benzene or (correspondingly) in acetic or propionic acid results in decarboxylation of the salt, with the formation of the organometallic compound.

$$RCOOHgOCOR \xrightarrow{h\nu} RHgOCOR + CO_2 \qquad (1)$$
$$R = CH_3 \text{ or } C_2H_5.$$

The yields of the organometallic compounds reached 66-68%, and the reaction was of preparative interest.

In this paper we studied the photoreaction of mercuric n-butyrate for the purpose of determining whether the compound can be used for the synthesis of n-propylmercury salts. The mercuric n-butyrate was irradiated in benzene at 80°. The experimental results are given in the table.

The highest yield (53.2%) of n-propylmercury salts was obtained when the reaction mass was irradiated for 2.5 hr with stirring (Expt. 2). Nearly all of the starting salt reacted under these conditions. The reaction products were found to contain, besides the organometallic compound, also the mercurous salt and a small amount of metallic mercury. With a longer time of irradiation (Expt. 3) the yield of the n-propylmercury salt was only 24.6%; there was a corresponding increase in the yields of mercurous salt and metallic mercury. A substantial portion of the starting mercury salt (33.8%) failed to react when the time of irradiation was insufficient (Expt. 1). The yields of n-propylmercury salts and mercurous salt were lower than in Expt. 2. Metallic mercury was absent in the reaction products. The liberated gas consisted of CO_2, propane and propylene. The amount of liberated gases, especially of the hydrocarbons, increased with increase in the length of irradiation.

From the obtained data it is possible to conclude that in general the photodecarboxylation of mercuric n-butyrate proceeds by the scheme proposed earlier [1] for the photoreactions of mercuric acetate and mercuric propionate. That the reaction has a chain free-radical character is supported by the fact that gas evolution was observed for some time after irradiation of the reaction mass had been discontinued.

The photoreaction of mercuric n-butyrate in benzene differs from the photoreactions of mercuric acetate and mercuric propionate in that it is more rapid and goes to a greater extent. To complete the photoreaction of mercuric acetate in benzene required 5-7 hr, while that of mercuric propionate required 3-3.5 hr [1]. The reaction products were stable to further irradiation, and the evolution of gas ceased completely. In the case of mercuric n-butyrate practically all of the salt had reacted within 2.5 hr after the start of irradiation; on further irradiation the reaction products decomposed to mercurous n-butyrate and metallic mercury, and a cessation of gas evolution was not observed (Expts. 2 and 3).

The mercuration of benzene by the mercuric n-butyrate was not observed during the photoreaction.

Photochemical Decarboxylation of Mercuric n-Butyrate in Benzene at 80° (in all of the experiments we used 150 ml of benzene)

Expt. No.	Amount of mercuric n-butyrate taken for reaction (in moles)	Time of irradiation (in min)	Obtained after reaction										
			n-propylmercury salt*		mercuric salt**		mercurous salt***		metallic mercury		CO_2	C_3H_8	C_3H_6
			(g)	yield (in %)	(g)	yield (in %)	(g)	yield (in %)	(g)	yield (in %)	(in moles)		
1	0.0267	46	3.93	39.7	2.10	33.8	1.36	21.5	0	0	0.0126	Not determined	
2	0.025	155	4.93	53.2	0.169	2.9	2.25	38.1	0.023	0.5	0.0232	0.0023	0.0006
3	0.020	278	1.82	24.6	0.07	1.5	2.74	58.0	0.38	9.5	0.0203	0.0024	0.0011

* Isolated as C_3H_7HgI.

** Isolated as HgS.

*** Isolated as Hg_2Cl_2.

EXPERIMENTAL

Reagents. The mercuric n-butyrate was prepared from sodium n-butyrate and analytically pure mercuric nitrate.

Found %: Hg 54.04, 53.81. $C_8H_{14}O_4Hg$. Calculated %: Hg 53.55.

Thiophene-free benzene was used, and it was distilled from sodium immediately before experiment.

The reactions were run in the earlier-described apparatus [1]. A PRK-4 lamp served as the source of ultraviolet light. To obtain mixing of the reaction mass the flask was heated from below* in Expts. 2 and 3. The reaction mass was not stirred in Expt. 1. In Expt. 3 the lamp was turned off in 6.5 min after the start of irradiation (300 ml of gas had evolved); the boiling of the reaction mass was continued; gas evolution was observed for 1 min after turning off the lamp (25 ml of gas was evolved). After 10 min the lamp was turned on again.

At the end of irradiation the system was blown with air, as described earlier [1]. The evolved gas was analyzed in the same manner as indicated earlier [1].

The reaction mass after cooling was filtered, and the precipitate was washed with benzene. The precipitate was a mixture of mercuric and mercurous butyrates and metallic mercury. To separate the mixture, a part of the precipitate was digested with dilute 1:1 hydrochloric acid, and the mercuric salt was precipitated from the solution as HgS. A second portion of the precipitate was treated with dilute nitric acid, and the metallic mercury was removed from the solution by filtration. The addition of KCl to the filtrate caused the mercurous salt to precipitate as mercurous chloride. The benzene solution was washed with a little water, and then the benzene was removed by distillation. The residue was dissolved in ether, and the solution was repeatedly extracted with water. Treatment of the extract with KI gave a precipitate of C_3H_7HgI; m.p. 110-111° (from methanol). The aqueous solution obtained in washing the benzene solution was treated with NaCl. The obtained precipitate of mercurous chloride was filtered, and the filtrate was treated with excess KI to dissolve the precipitated HgI_2. A small amount of C_3H_7HgI was removed from the solution; m.p. 110-111° (from methanol). The filtrate was saturated with H_2S, and the obtained precipitate of HgS was filtered. Evaporation of the water-washed ether solution left a small amount (0.2-0.5 g) of oil with a disagreeable odor. The oil was not investigated further.

SUMMARY

1. The photoreaction of mercuric n-butyrate in benzene was studied at 80°. It was shown that decarboxylation of the salt occurs here with the formation of n-propylmercury butyrate in 53% yield. In addition, the reaction products were found to contain mercurous n-butyrate, metallic mercury, CO_2, propane and propylene.

* Without additional heating, a boiling and mixing of the reaction mass was observed only above the tube sealed in the quartz flask, in which the PRK-4 lamp was placed.

2. The photoreaction of mercuric n-butyrate can serve as a convenient method for the synthesis of n-propylmercury salts.

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SOME SUBSTITUTED 2-ARYL-5-ARYLIDENE-1-IMIDAZOLIN-4-ONES

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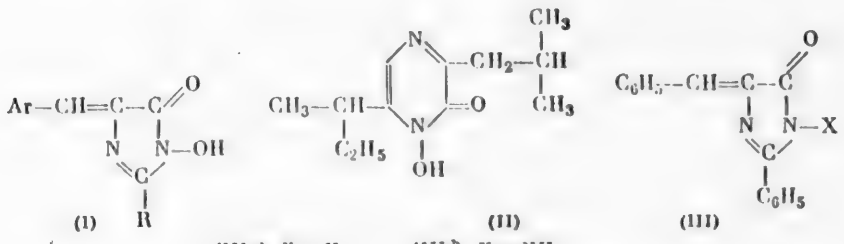
The 2-substituted 5-arylidene-1-imidazolin-3-ol-4-ones (I), obtained recently in our laboratory [1], exhibit an antibacterial action that, like that of other hydroxylamine derivatives, is highly specific [2-4] and especially effective against bacteria of the intestinal group and Mic. tuberculosis. Since the indicated compounds have a structural similarity to aspergillic acid (II), the thought naturally arose that the action of the imidazolinolones (I) is linked with the presence of the N-hydroxy group in their molecule, which, as is known [5], determines the antitubercular action of aspergillic acid. To verify this theory we synthesized a number of previously unknown derivatives of 2-phenyl-5-benzylidene-1-imidazolin-4-one, substituted on the nitrogen in the 3 position (III).



(I) (II) (III)

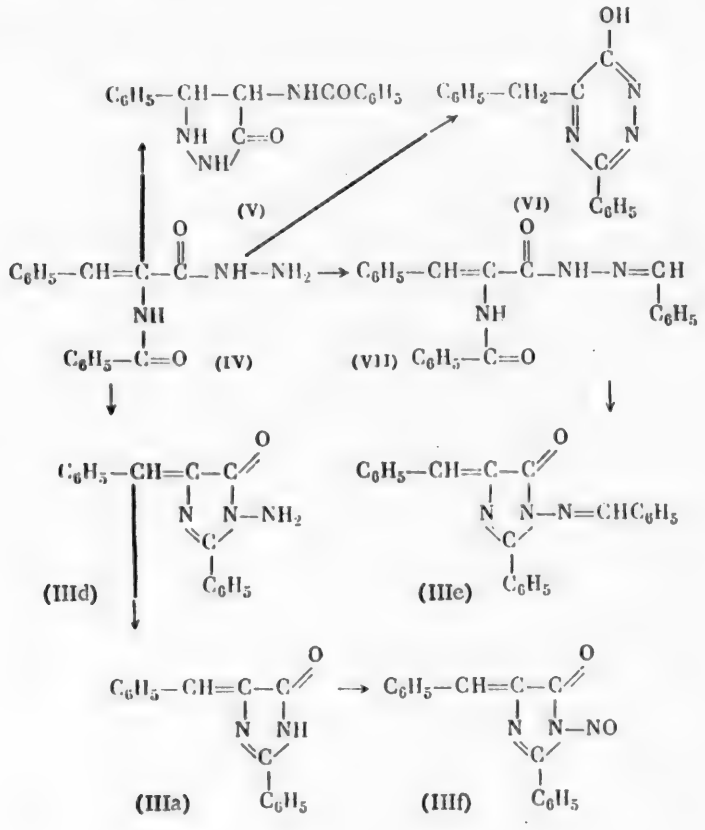
(IIIa) X = H, (IIIb) X = OH, (IIIc) X = OCH_3, (IIId) X = NH_2, (IIIe) X = $N{=}CHC_6H_5$, (IIIf) X = NO.

The synthesis of 2-aryl-5-arylidene-1-imidazolin-4-ones (III) has been discussed many times in the literature. Usually the synthesis is accomplished by the cyclization of N-substituted amides of α-acylaminocinnamic acids. Depending on the nature of the substituent, the cyclization is carried out using either alkaline [6, 7] (IIIa) or acid (IIIb) agents [1], or thermally (III, X = R) [8]. If X = CHRR', then in general the cyclization cannot be accomplished [9].

Besides the earlier described [1] 3-hydroxy- and 3-methoxy-2-phenyl-5-benzylidene-1-imidazolin-4-ones (IIIb and IIIc), we synthesized the 3-amino-, 3-benzylideneamino and 3-nitroso-2-phenyl-5-benzylidene-1-imidazolin-4-ones (IIId, IIIe and IIIf).

To obtain the 3-amino derivative (IIId) we studied the cyclization of α-benzamidocinnamic acid hydrazide (IV). As is known, when the hydrazide of α-benzamidocinnamic acid is treated with alkaline agents, only pyrazolidinones (V) or triazines (VI) are formed [10, 11], while treatment with acid agents leads to decomposition of the hydrazides [11]. However, we were able to show that the cyclization of α-benzamidocinnamic acid hydrazide

can be directed toward the formation of imidazolinone derivatives. Thus, dehydration by azeotropic distillation with toluene gave us (IIId), the yield of which, however, was only 10%, since also in this case the reaction went mainly toward the formation of pyrazolidinones and triazines.



To improve the synthesis of (IIId) we cyclized the benzylidenehydrazide of α-benzamidocinnamic acid (VII) to the benzylideneimino derivative (IIIe). Benzylidenehydrazide (VII), obtained in high yield by the condensation of α-benzamidocinnamic acid hydrazide (IV) with benzaldehyde, when treated with hydrobromic acid, or even better when heated with phosphorus oxychloride [12], is cyclized in high yield to the imidazolinone (IIIe). All attempts to hydrolyze this compound to the amino derivative (IIId) (refluxing in alcohol, saturated with hydrogen chloride, refluxing with concd. hydrochloric acid, etc.) proved unsuccessful. The azomethine bond proved to be unusually stable to hydrolysis.

It is interesting that we were also unable to effect the reverse reaction, i.e., obtain the benzylideneimino derivative (IIIe) from (IIId). The latter failed to react with benzaldehyde in the presence of various agents. Even refluxing (IIId) in benzaldehyde failed to achieve the desired purpose.

The peculiar character of the amino group found in the 3 position of the imidazolinone ring is also manifested in its other properties. Thus, it is an extremely weak base ($K_b < 10^{-12}$). We studied the diazotization of the amino group in (IIId); it proved that this reaction does not go normally in aqueous hydrochloric or sulfuric acid. Only when the sodium nitrite is added to a hot solution of the amino derivative (IIId) in glacial acetic acid does deamination occur, resulting in the formation of 2-phenyl-5-benzylidene-1-imidazolin-4-one (IIIa). A similar deamination was known earlier for the case of the aminopyrazolinones [13-15]. The use of excess sodium nitrite yields 3-nitroso-2-phenyl-5-benzylidene-1-imidazolin-4-one (IIIf), obtained by the nitrosation of the initially formed (IIIa). This was shown by the direct nitrosation of an authentic sample of (IIIa) under the same conditions.

The reason for the amino group in the 3 position of the imidazolinone ring showing so many unusual properties is probably due to the fact that this amino group is, on the one hand, the amino group of an unsymmetrical diacylhydrazine, and on the other hand, because the free pair of electrons of the nitrogen atom is drawn into reaction with the carbonyl and amidine groups of the ring. As a result of this the basic properties of the amino group in (IIId) are weakened, and the ability to form a new [in the case of (IIId)] or to cleave an already existing [in the case of (IIIe)] azomethine linkage is suppressed.

The compounds obtained by us [(IIId), (IIIe) and (IIIf)], as well as those described earlier (IIIa) [6] and (IIIc) [1], proved to be completely devoid of antibacterial activity, which supports the validity of our theory that it is necessary to have a N-hydroxy group present in the imidazolinone ring in order to obtain physiological activity. However, this does not mean that the mechanism of the antibacterial action of our earlier-described [1] 2-aryl-5-arylidene-1-imidazolin-3-ol-4-ones is similar to the mechanism of the antitubercular action of aspergillic acid. For the latter it was both proposed [5] and shown [16] that its activity is connected with the removal of heavy metals, in particular of iron, from the metabolic processes essential for the life activity of Mic. tuberculosis, due to the formation of complexes.

A study of the absorption spectra of the imidazolinolones (I) in the presence of heavy metal ions revealed that the imidazolinolones do not form complexes with metals; in particular, with copper and iron. This gives us a basis to assume that the mechanism of the antibacterial action of the imidazolinolones (I) differs from the mechanism of the action of aspergillic acid, and most probably reduces to the fact that (I) acts as a special kind of hydroxamic acid on certain fermentive systems [17-19].

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EXPERIMENTAL

α-Benzamido-β-phenylacrylic acid hydrazide (IV). A solution of 20 g of hydrazine hydrate in 500 ml of methanol, acidified to pH 6 with acetic acid, was added to 25 g of 2-phenyl-4-benzylidene-2-oxazolin-5-one. The yellow precipitate of azlactone went into solution, and after 30-40 min the hydrazide began to deposit as cubic crystals. After 3 hr the precipitate was filtered and washed with methanol and ether. Yield 18 g (64%), m.p. 158-159°. The mother liquor was evaporated in vacuo to a volume of 80-100 ml and then alkalized to pH 7-7.2 with aqueous caustic solution. Here we obtained 8.6 g (28%) of the hydrazide monohydrate, m.p. 148-150°. Total yield 92%. Literature data: m.p. of anhydrous hydrazide 157-158° [20], of the monohydrate 151-153° [10].

α-Benzamido-β-phenylacrylic acid benzylidenehydrazide (VII). A solution of 14 g of α-benzamido-β-phenylacrylic acid hydrazide in 100 ml of methanol was prepared by heating, and then 6 g of benzaldehyde was added. The solution was stirred without heating for 1.5-2 hr, after which the obtained white crystalline precipitate was filtered and washed with methanol and ether. Yield 16.3 g (89%), m.p. 231-232°.

Found %: N 11.15. $C_{23}H_{19}O_2N_3$. Calculated %: N 11.11.

3-Amino-2-phenyl-5-benzylidene-1-imidazolin-4-one (IIId). A suspension of 5 g of α-benzamido-β-phenylacrylic acid hydrazide monohydrate in 150 ml of toluene was distilled to remove the water as an azeotropic mixture, and then at the end evaporated in vacuo to dryness. The residue was dissolved in 100 ml of hot alcohol. After a day 0.5 g (11%) of 3-amino-2-phenyl-5-benzylidene-1-imidazolin-4-one deposited as yellow needle crystals with m.p. 192-193°.

Found %: C 72.79; H 4.97; N 15.92. $C_{16}H_{13}ON_3$. Calculated %: C 72.98; H 4.94; N 15.97.

A mixture of 5-phenyl-4-benzamido-3-pyrazolidinone (V) and 3-phenyl-5-benzyl-6-hydroxy-1,2,4-triazine (VI) was isolated from the mother liquor (see [11]).

3-Benzamido-2-phenyl-5-benzylidene-1-imidazolin-4-one (IIIe). a) A solution of 3.7 g of α-benzamido-β-phenylacrylic acid benzylidenehydrazide in 37 ml of acetic acid, containing 0.8 g of hydrogen bromide, was refluxed for 5 minutes. A copious white precipitate deposited, which after cooling was filtered and washed with alcohol and ether. Yield 2.4 g (68%), m.p. 182-183° (from a mixture of alcohol and chloroform).

b) A suspension of 7.4 g of α-benzamido-β-phenylacrylic acid benzylidenehydrazide in 50 ml of chloroform was treated with 15 ml of phosphorus oxychloride, and then the mixture was refluxed on the water bath for

3-4 hr. The clear, pale-yellow reaction mixture was poured over ice, after which the chloroform layer was separated, washed with sodium carbonate solution, dried, and evaporated to a volume of 20 ml. The residue was treated with 25-30 ml of alcohol and the mixture rubbed until crystallization started. The obtained crystals were filtered and washed with alcohol. Yield 6.8 g (96%).

Found %: C 78.68; H 5.02. $C_{23}H_{17}ON_3$. Calculated %: C 78.61; H 4.84.

2-Phenyl-5-benzamido-1-imidazolin-4-one (IIIa). A solution of 0.25 g of 3-amino-2-phenyl-5-benzylidene-1-imidazolin-4-one in 30 ml of hot acetic acid was treated with 0.09 g of sodium nitrite and then the mixture was heated on the boiling water bath for 30 min. Then the mixture was cooled, diluted with 100 ml of water, and the obtained precipitate was filtered and then recrystallized from the minimum amount of acetic acid. The compound was obtained as yellow plates with m.p. 270-272°. The mixed melting point with authentic 2-phenyl-5-benzylidene-1-imidazolin-4-one [7] was not depressed.

3-Nitroso-2-phenyl-5-benzylidene-1-imidazolin-4-one (IIIf). A solution of 0.5 g of 3-amino-2-phenyl-5-benzylidene-1-imidazolin-4-one in 50 ml of hot acetic acid was treated with 0.69 g of sodium nitrite and the mixture heated at 100° for 1 hr. The mixture was cooled to give 0.18 g (37%) of a yellow crystalline precipitate with m.p. 263-265°. The same compound was obtained in 55% yield by the nitrosation of authentic 2-phenyl-5-benzylidene-1-imidazolin-4-one under similar conditions.

Found %: N 15.09. $C_{16}H_{11}O_2N_3$. Calculated %: N 15.20.

SUMMARY

1. Some derivatives of 2-phenyl-5-benzylidene-1-imidazolin-4-one were obtained, containing substituents on the nitrogen in the 3 position.

2. The mechanism of the antibacterial action of 2-arylidene-1-imidazolin-3-ol-4-ones was discussed.

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THE STEREOCHEMISTRY OF AZLACTONES

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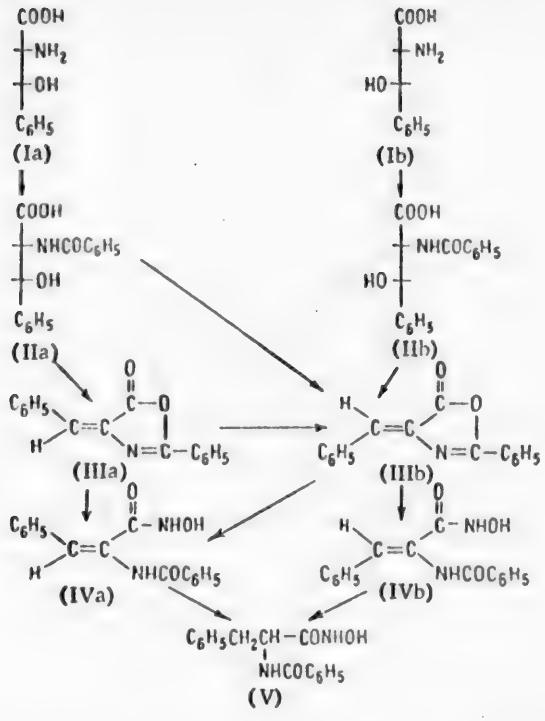
In studying the reaction of azlactones with hydroxylamine, serving as a base for the development of a method of synthesis of α-acylamino-β-arylacryloylhydroxamic acids [1], we observed that the melting point of the obtained unsaturated hydroxamic acids changes substantially depending on the reaction conditions used. Thus, when 2-phenyl-4-benzylidene-2-oxazolin-5-one is reacted with hydroxylamine (free base) at 20-25° or with hydroxylamine acetate at 50° the obtained α-benzoylamino-β-phenylacryloylhydroxamic acid has m.p. 125-127°; reaction of the same oxazolinone with hydroxylamine acetate in the cold gives a hydroxamic acid with m.p. 106-107°. Since repeated purification of both specimens failed to change the melting point, while their catalytic hydrogenation led to the same N-benzoyl-β-phenylalanylhydroxamic acid, it was natural to assume that the difference in the two specimens of unsaturated hydroxamic acid obtained by us could be due to cis-trans isomerism.

Since the opening of the oxazolinone ring by the hydroxylamine does not involve the semicyclic double bond, then it is obvious that the geometric isomerism of the formed unsaturated hydroxamic acids under sufficiently mild reaction conditions, excluding isomerization of the double bond, should correspond to the geometric isomerism of the starting azlactones. As a result, these two problems are closely related, and in this paper we present data that enable arriving at a definite conclusion as to the configuration of the two isomers of 2-phenyl-4-benzylidene-2-oxazolin-5-one and the hydroxamic acids formed from them

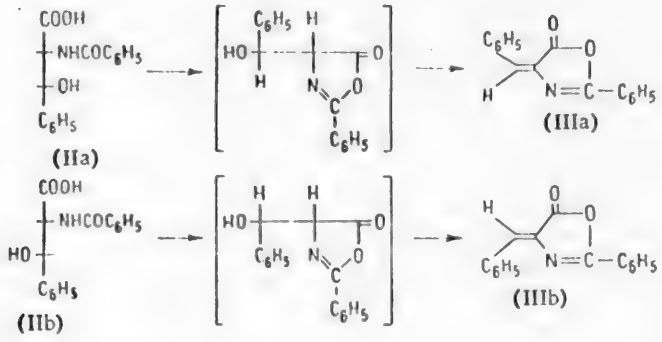
Despite the large number of papers devoted to the chemistry of azlactones, the problem as to their stereochemistry remains unsolved. In some cases [2-4] the azlactones were isolated in two forms, but the data given by the authors did not permit making any definite conclusions as to the stereochemistry. The closest to solving the problems were Carter and Risser [7], who obtained the two isomers of 2-phenyl-4-benzylidene-2-oxazolin-5-one from the two diastereomeric O-methyl-N-benzoyl-β-phenylserines, one of which (m.p. 167-168°), also obtained by the Erlenmeyer synthesis from the azlactone, was more stable, while the second (m.p. 148-150°) was easily converted to the high-melting isomer by treatment with bases. Although it was shown on the basis of the hydrolysis and alcoholysis results that the isomerism exhibited by the azlactones is of the cis-trans type, still a definite configuration could not be assigned to them.

To solve this problem we synthesized both of the isomeric 2-phenyl-4-benzylidene-2-oxazolin-5-ones; here, since according to the data of Carter [6] the mechanism for the formation of azlactones from β-hydroxy-, β-alkoxy- and β-acyloxy-α-acylamino acids proceeds by a different mechanism, we started with the β-phenylserines, the configuration of which had been rigidly established [7-10].

The benzoylation of erythro-β-phenylserine (Ia) and its threo-isomer (Ib) under mild conditions gave erythro-N-benzoyl-β-phenylserine (IIa) and threo-N-benzoyl-β-phenylserine (IIb), respectively. The stable isomer of 2-phenyl-4-benzylidene-2-oxazolin-5-one with m.p. 167-168° (IIIb) is formed in good yield when the threo-isomer (IIb) is heated with acetic anhydride for a short time. The erythro-isomer (IIa) under the same conditions gives the labile azlactone (IIIa) with m.p. 148-150° together with (IIIb), in which connection the amount of the latter increases the longer the heating, due to conversion of (IIIa) to (IIIb), which takes place under the reaction conditions [5].



Since the unsaturated azlactones are formed from N-benzoyl-β-phenylserine through the intermediate unsaturated hydroxylactone [11], then in the final analysis the configuration of the formed unsaturated azlactone is determined by the stereochemical course of the cleavage of a water molecule from the intermediate product. Since this process should proceed via trans-elimination,• it must be assumed that the threo-N-benzoyl-β-phenylserine (IIb) should give the trans-azlactone (IIIb), while the erythro-isomer (IIa) should give the cis-azlactone (IIIa).••



The greater stability of the trans-azlactone (IIIb) when compared with the cis-isomer (IIIa) must primarily be explained by the stronger stabilization of the (IIIb) configuration due to a more complete conjugation of the phenyl ring with the carbonyl group than with the azomethine linkage. It is well known that such conjugation is manifested much more clearly for groupings found in the trans-position to each other. Our theory regarding the

• The trans rule should be observed in the case of E_2-elimination. However, also in the case of E_1-elimination it is hardly possible to assume the formation of a stable carbanion; consequently, also in this case the process should proceed mainly via trans-elimination [12].

•• We determine the cis-trans isomerism of the azlactones by the mutual arrangement of the phenyl ring and the carbonyl group of the azlactone ring at the semicyclic double bond.

configuration of the obtained isomeric azlactones, in itself lacking sufficient proof, found complete confirmation in the properties of the stereoisomeric unsaturated hydroxamic acids formed from the azlactones. Two isomeric α-benzoylamino-β-phenylacryloylhydroxamic acids with m.p. 125-127° (IVa) and 106-107° (IVb) are formed respectively when (IIIa) and (IIIb) are reacted with hydroxylamine acetate at room temperature.

Running the reaction with hydroxylamine acetate at elevated temperature (50°) leads to the formation of the more stable isomer with m.p. 125-127° (IVa) from (IIIb), which is also obtained from (IIIb) by treating it in the cold with hydroxylamine (free base). The catalytic hydrogenation of (IVa) and (IVb), using palladium deposited on barium sulfate [1] as the catalyst, gives the same N-benzoyl-β-phenylalanylhydroxamic acid, and consequently (IVa) and (IVb) are geometric isomers.

Since the absence of isomerization at the semicyclic double bond of the azlactone could be expected under mild reaction conditions (hydroxylamine acetate at room temperature), then obviously, starting with the earlier adopted conjectural configuration for the starting azlactones, the cis-configuration must be assigned to the high-melting isomer (IVa), and the trans-configuration to isomer (IVb). We determine the configuration of the α-benzoylamino-β-phenylacryloylhydroxamic acids by the mutual arrangement of the phenyl ring and the hydroxamic grouping at the double bond.

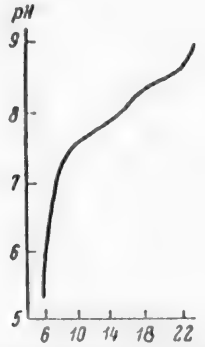


Fig. 1. Potentiometric titration curve of trans-α-benzoylamino-β-phenylacryloylhydroxamic acid.

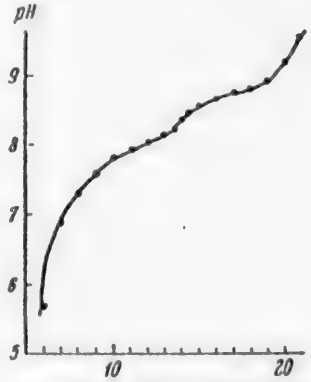


Fig. 2. Potentiometric titration curve of cis-α-benzoylamino-β-phenylacryloylhydroxamic acid.

To obtain experimental confirmation of the configurations adopted by us for (IVa) and (IVb) [and likewise (IIIa) and (IIIb)] we made resort to the potentiometric titration data. Assuming that a greater transfer of influence across the double bond occurs in the case of trans-position, it could be expected, in accordance with the configuration given above, that the acidity constant for the hydroxamic grouping (K_1) will be greater for the trans-isomer (IVb) than for the cis-isomer (IVa). On the other hand, the acidity constant of the benzoylamino group (K_2) will be greater for the cis-isomer, since in this isomer the phenyl ring and the benzoylamino group are found trans to each other. This assumption was fully confirmed by the experimental data. Potentiometric titration of the two isomers gave $pK_1 = 7.9$ and $pK_2 = 8.4$ for (IVa), and $pK_1 = 7.6$ and $pK_2 = 8.7$ for (IVb) (see Figs. 1 and 2).

As can be seen, the ratio of the acidity constants of the hydroxamic and benzoylamino groupings in the two isomers supports the fact that (IVa) has the cis-configuration, and (IVb) the trans-configuration. These data, proving the configuration of the obtained acids, at the same time support the configuration adopted by us for the starting 2-phenyl-4-benzylidene-2-oxazolin-5-ones: the high-melting isomer (IIIb) has the trans-configuration, while the low-melting isomer (IIIa) has the cis-configuration. As a result, we were the first to establish the configuration of the two geometric isomers of the azlactone.

These data also permit establishing the configuration of the diastereomeric O-methyl-β-phenylserines, used by Carter and Risser as starting materials for the synthesis of the isomeric azlactones [7]: the O-methyl-β-phenylserine isomer with m.p. 260° proved to be the erythro-isomer, while the isomer with m.p. 196° was the threo-isomer.

It should be mentioned that establishing the structure and configuration of the O-methyl-β-phenylserines by conversion to β-phenylserines of authentic configuration does not lead to success [14, 15].

EXPERIMENTAL

Erythro-N-benzoyl-β-phenylserine (IIa). A suspension of 10 g of the hydrochloride of the ethyl ester of erythro-β-phenylserine [12] in 150 ml of 2N methanolic KOH solution was stirred for 1 hr, after which it was evaporated in vacuo at 20° to a volume of 50-60 ml and the residue treated with 100 ml of water. The clear solution was cooled to -3 to 0° and then 15 ml of benzoyl chloride was added. After 2 hr the mixture was acidified at 0° with dilute hydrochloric acid to pH 4 and then extracted with ether. The ether extracts were washed with water, dried over sodium sulfate and then evaporated on the water bath, at the end under vacuum. The dry residue was refluxed with 100 ml of ether, cooled, and the precipitate was filtered and washed with ether. Yield 5.7 g (48%), m.p. 190-193°. Literature data [13]: m.p. 197-198°.

Threo-N-benzoyl-β-phenylserine (IIb). A solution of 9 g of threo-β-phenylserine [10] in 150 ml of 10% NaOH solution was treated at 0-5° with 20 ml of benzoyl chloride. At the end of reaction the solution was acidified at 0° with dilute hydrochloric acid, after which the obtained precipitate was filtered and washed with water and with ether. Yield 9.1 g (64%), m.p. 158-162°. After purification through the phenethylamine salt (m.p. 180-182°) the melting point of the pure threo-N-benzoyl-β-phenylserine was 161-162° (from aqueous alcohol).

Found %: N 5.06. $C_{16}H_{15}O_4N$. Calculated %: N 4.91.

Cis-2-phenyl-4-benzylidene-2-oxazolin-5-one (IIIa). A suspension of 4.4 g of erythro-N-benzoyl-β-phenylserine in 25 ml of acetic anhydride was heated on the boiling water bath for 8-10 min. A precipitate of 2.2 g of trans-2-phenyl-4-benzylidene-2-oxazolin-5-one was obtained on cooling; the filtrate was poured into 150 ml of ice water and stirred vigorously for 2 hr. The yield of crude cis-azlactone as a viscous yellow mass was 1.9 g, m.p. 110-125°. The substance was purified by conversion to α-benzoylaminocinnamic acid, and subsequent azlactonization with acetic anhydride [5] gave 1.1 g (28%) of cis-2-phenyl-4-benzylidene-2-oxazolin-5-one with m.p. 148-149°. Literature data [1,5]: m.p. 148-150°.

Trans-2-phenyl-4-benzylidene-2-oxazolin-5-one (IIIb). A suspension of 3 g of threo-N-benzoyl-β-phenylserine in 15 ml of acetic anhydride was heated for 5-10 min on the boiling water bath. The solution was poured into 100 ml of ice water, stirred for 1 hr, and the resulting precipitate separated by filtration. The yield of trans-2-phenyl-4-benzylidene-2-oxazolin-5-one was 2.4 g (92%), m.p. 166-167°. Literature data [5]: m.p. 166-168°.

Cis-α-benzoylamino-β-phenylacryloylhydroxamic acid (IVa). a) Ten grams of the 2-benzylideneoxazolin-5-one was added to 200 ml of a 0.5N methanolic solution of hydroxylamine acetate, warmed to 45-50°. After 4 hr the mixture was cooled to 10°, 200 ml of water was added, the whole kept at -10° for 16-20 hr, after which the obtained colorless precipitate was filtered, washed with water, ethyl acetate, and ether, and then reprecipitated (see [1]). Yield 4.7 g (42%), m.p. 125-127°. Literature data [16]: m.p. 126-128°.

b) Two grams of the cis-2-phenyl-4-benzylidene-2-oxazolin-5-one was dissolved in 40 ml of a 0.5N methanolic solution of hydroxylamine acetate. After 1.5 hr we isolated, as described above, 1.6 g (71%) of cis-α-benzoylamino-β-phenylacryloylhydroxamic acid with m.p. 125-127°.

c) Reaction of the trans-2-phenyl-4-benzylidene-2-oxazolin-5-one with hydroxylamine (free base) [14] gave the cis-α-benzoylamino-β-phenylacryloylhydroxamic acid in 50% yield, m.p. 125-127°. Reprecipitation fails to change the melting point; $pK_1 = 7.9$; $pK_2 = 8.4$ (see Fig. 2).

Trans-α-benzoylamino-β-phenylacryloylhydroxamic acid (IVb). Using the procedure described in b), we obtained 9.1-10.6 g (80-94%) of trans-α-benzoylamino-β-phenylacryloylhydroxamic acid with m.p. 106-107° from 10 g of trans-2-phenyl-4-benzylidene-2-oxazolin-5-one; $pK_1 = 7.6$; $pK_2 = 8.7$ (see Fig. 1).

Hydrogenation of cis- and trans-α-benzoylamino-β-phenylacryloylhydroxamic acids. A solution of 2.8 g of cis-α-benzoylamino-β-phenylacryloylhydroxamic acid (m.p. 125-127°) in 50 ml of methanol was hydrogenated in a goose-necked bottle using 5% palladium-on-$BaSO_4$ as the catalyst. One mole of hydrogen was absorbed within an hour. The catalyst was filtered, while the filtrate was evaporated to a volume of 15-20 ml and then treated with 50 ml of water. After 12 hr at -10° we obtained 2.5 g (88%) of N-benzoyl-β-phenylalanylhydroxamic acid (V) with m.p. 146-147°. The substance is readily soluble in alcohol and acetone, gives a characteristic color with ferric chloride solution, and decolorizes Fehling solution.

Employing similar conditions, we obtained 2.53 g (91%) of N-benzoyl-β-phenylalanylhydroxamic acid with m.p. 146-147° from 2.8 g of trans-α-benzoylamino-β-phenylacryloylhydroxamic acid (m.p. 106-107°), which proved to be identical with the compound obtained from the hydrogenation of the cis-isomer.

SUMMARY

1. The configuration of the stereoisomeric 2-phenyl-4-benzylidene-2-oxazolin-5-ones was determined, which is the first example of establishing the configuration of unsaturated azlactones.

2. The configuration of the stereoisomeric α-benzoylamino-β-phenylacryloylhydroxamic acids was established.

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*Original Russian pagination. See C. B. Translation.

THE INTERACTION OF KETENE WITH NITROGEN-CONTAINING BASES

VIII. CHLOROACETYLATION OF PRIMARY AROMATIC AMINES

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Bashkir State University
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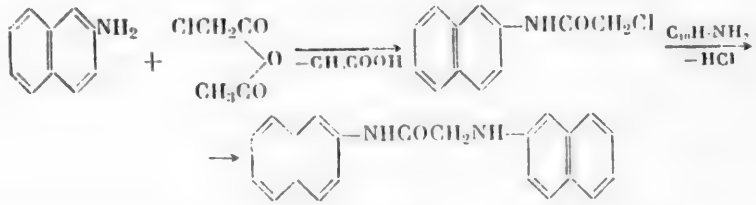
Original article submitted July 2, 1959

In the preceding communication one of us put forward a method of chloroacetylation of amines using ketene and monochloroacetic acid [1]. It was subsequently found that the method justifies itself over a wide range of basicities of aromatic amines. For example, o-nitroaniline with a dissociation constant of $K_{25} = 0.56 \cdot 10^{-14}$ is chloroacetylated just as easily as β-naphthylamine with $K_{25} = 0.2 \cdot 10^{-9}$. Difficulties are encountered in the isolation of the chloroaceto derivatives in the pure form. It was found, however, that the reaction products are separated with facility in a medium of aqueous alcohol or acetic acid.

Chloroacetylation of amines by acid chlorides should preferably be performed with a ratio of one mole of chloroacetyl chloride to two moles of amine [2], since it is essential that the hydrogen chloride should be bound by the excess of amine to form the corresponding salt. This ratio proved unsuitable for chloroacetylation with the mixed anhydride of chloroacetic and acetic acids. The anticipated chloroacetonaphthalide is not formed if two moles of β-naphthylamine are taken per mole of monochloroacetic acid; the main product of the reaction is N-(β-naphthylglycine)-β-naphthylamine, and unchanged β-naphthylamine is recovered. This reaction course is a consequence of the chloroacetonaphthalide entering into further condensation due to the very high lability of the chlorine atom.



A similar picture is observed with α-naphthylamine and other amines. The most favorable ratio is 0.7 mole of amine per mole of chloroacetic acid; the yield of chloroaceto derivatives then varies between 50 and 70% calculated on the original amine.

EXPERIMENTAL

The mixed anhydride of monochloroacetic and acetic acids was prepared by passage of ketene into chloroacetic acid. The reaction was considered at an end when the acid had dissolved completely and heat was not liberated. The resulting mixture was used for the subsequent syntheses without fractional distillation.*

* Check experiments run with the pure mixed anhydride did not lead to higher yields of reaction products.

α-Chloroacetonaphthalide. Ketene was passed into 10 g of monochloroacetic acid until the mixed anhydride had been formed. The solution was run into 10 g of α-naphthylamine and the latter dissolved completely. Reaction temperature 87°. After cooling, the reaction mixture crystallized completely; the crystals were washed many times on the filter with hot water. Yield 9.3 g (60%) of α-chloroacetonaphthalide with m.p. 160-161° (from alcohol).*

Found %: Cl 16.20. $C_{12}H_{10}ONCl$. Calculated %: Cl 16.14.

β-Chloroacetonaphthalide. The mixed anhydride from 10 g of monochloroacetic acid was run into 10 g of β-naphthylamine. The resulting crystals were washed with hot water and then boiled in 150 ml of water (a large part remained in the form of a heavy oily layer). Alcohol was run into the boiling solution until the oil had dissolved. The solution was filtered and 30 ml of water was added to the filtrate. The resulting voluminous, white precipitate was filtered, washed with warm water and dried at 100°. Yield 8.4 g (55%) of β-chloroacetonaphthalide with m.p. 116-118°.

Found %: Cl 16.21. $C_{12}H_{10}ONCl$. Calculated %: Cl 16.14.

N-(β-Naphthylglycine)-β-naphthylamide. To 14 g of β-naphthylamine was added the mixed anhydride prepared from 5 g of monochloroacetic acid. The product was washed many times and recrystallized from aqueous alcohol. Yield 4.5 g of N-(β-naphthylglycine)-β-naphthylamide with m.p. 171-173°, in agreement with Beilstein [3]. The amount of β-naphthylamine recovered was 10 g. Chloroacetonaphthalide was not detected.

p-Nitrochloroacetanilide. The anhydride prepared from 5 g of chloroacetic acid was mixed with 4.6 g of p-nitroaniline. The temperature rose spontaneously to 85° and the crystals dissolved. After cooling, the mixture crystallized. After preliminary washing with water, the reaction product was washed and recrystallized from concentrated acetic acid in presence of carbon. Yield 4.1 g (58%) of p-nitrochloroacetanilide with m.p. 181-183°.

Found %: Cl 16.65. $C_8H_7O_3N_2Cl$. Calculated %: Cl 16.52.

m-Nitrochloroacetanilide. The anhydride prepared from 5 g of chloroacetic acid was mixed with 4.6 g of m-nitroaniline. Reaction temperature 73°. After cooling, the mixture crystallized within a few hours. Washing with hot water and crystallization from alcohol gave 5.7 g (76.7%) of m-nitrochloroacetanilide with m.p. 110-111°.

Found %: Cl 16.34. $C_8H_7O_3N_2Cl$. Calculated %: Cl 16.52.

o-Nitrochloroacetanilide. The anhydride prepared from 5 g of monochloroacetic acid was mixed with 4.6 g of o-nitroaniline. The crystals went into solution and later the mixture crystallized. Yield 4.6 g (64.3%) of o-nitrochloroacetanilide with m.p. 87-89° (from acetic acid).

Found %: Cl 15.74. $C_8H_7O_3N_2Cl$. Calculated %: Cl 16.52.

m-Bromochloroacetanilide. The anhydride prepared from 4.7 g of chloroacetic acid was mixed with 6 g of m-bromoaniline. Considerable heat was liberated. The resulting crystals were washed and crystallized from an alcoholic aqueous medium. Yield 4.9 g (56.4%) of m-bromochloroacetanilide with m.p. 113-114°.

Found %: Cl 14.08. $C_8H_7ONClBr$. Calculated %: Cl 14.27.

p-Bromochloroacetanilide. The anhydride prepared from 4.7 g of chloroacetic acid was mixed with 6 g of p-bromoaniline. Reaction temperature 83°. The cooled reaction mixture deposited crystals which were washed with water and recrystallized from an aqueous alcoholic medium. Yield 4.74 g (56%) of p-bromochloroacetanilide with m.p. 179-182°.

Found %: Cl 14.07. $C_8H_7ONClBr$. Calculated %: Cl 14.27.

m-Chlorochloroacetanilide. The anhydride prepared from 10 g of monochloroacetic acid was mixed with 9 g of m-chloroaniline. Reaction temperature 71°. The cooled mixture crystallized after a few hours. The crystals were washed with water and crystallized from an alcoholic medium. Yield 7.5 g (54%) of m-chlorochloroacetanilide with m.p. 96-98°.

Found %: Cl 16.88. $C_8H_7ONCl_2$. Calculated %: Cl 17.37.

* In all cases the melting points of the chloroaceto derivatives agreed with the Beilstein data.

SUMMARY

A series of chloroaceto derivatives of aromatic amines was prepared by a new chloroacetylation reaction.

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SYNTHESIS OF SOME ESTERS OF PHOSPHINIC, MONOTHIO- AND DITHIO-PHOSPHORIC ACIDS CONTAINING THE MYRTENYL RADICAL

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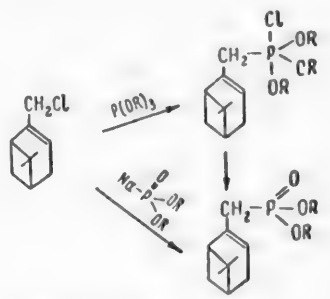
Terpenic derivatives of phosphinic, monothio- and dithiophosphoric acids have been little studied, but they present interest since products of reaction of diesters of dithiophosphoric acids and terpenes possess insecticidal [1] and other valuable properties [2]. No data are available for derivatives of the above acids containing the myrtenyl radical.

In the present work we studied the reactions of myrtenyl chloride with trialkyl phosphites, which proceed in accordance with the A. E. Arbuzov mechanism and lead to formation of dialkyl esters of myrtenylphosphinic acid.

The same dialkyl esters of myrtenylphosphinic acid were prepared by reaction of myrtenyl chloride with sodium dialkyl phosphites.

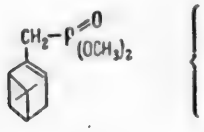
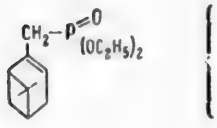
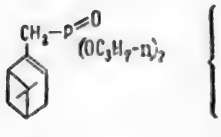
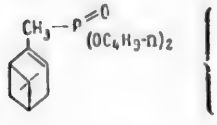
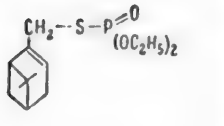
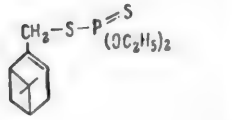


R = CH_3, C_2H_5, n-C_3H_7; n-C_4H_9

All these esters are colorless, nearly odorless, readily distillable, oily liquids, soluble in organic solvents and insoluble in water.

Reaction of myrtenyl chloride with sodium diethyl monothiophosphate gave the myrtenyldiethyl ester of monothiophosphoric acid in the form of an orange-colored, oily liquid with a characteristic odor of roast onion. The reaction mixture decomposed during fractionation, and this accounts for the poor yield of ester, although the pure product distils without decomposition.

The myrtenyldiethyl ester of dithiophosphoric acid is obtained in better yield in the form of a light-yellow, oily liquid with an unpleasant odor.

Compound prepared	Starting substances reacting with myrtenyl chloride	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}
	$(CH_3O)_3P$	128—130° (4.5)	1.4833	1.0962
	$(CH_3O)_2PONa$	117 (2)	1.4828	1.0971
	$(C_2H_5O)_3P$	117—118 (1)	1.4755	1.0487
	$(C_2H_5O)_2PONa$	138 (4)	1.4750	1.0492
	(n.-$C_3H_7O)_3P$	138—139 (1)	1.4723	1.0149
	(n.-$C_3H_7O)_2PONa$	141 (2)	1.4722	1.0152
	(n.-$C_4H_9O)_3P$	166—167 (3)	1.4720	1.0042
	(n.-$C_4H_9O)_2PONa$	165 (2.5)	1.4720	1.0045
	$(C_2H_5O)_2POSNa$	165—166.5 (2.5)	1.5042	1.0922
	$(C_2H_5O)_2PS_2Na$	159 (2.5)	1.5325	1.1009

The physical constants of the compounds obtained and their analytical data are set forth in the table.

EXPERIMENTAL

Myrtenyl chloride. The compound prepared by D. V. Tishchenko's method [3] had b.p. 59° at 3.5 mm, nD^{20} 1.4952, d_4^{20} 1.0146.

Reaction with trimethyl phosphite. A mixture of 10 g of myrtenyl chloride and 7.4 g of trimethyl phosphite in a sealed tube was heated for 9 hr at 130-140°. The volume decreased appreciably on cooling. Continuation of heating at 150° for a day led to increase in volume in the tube (evidence of partial decomposition of the reaction products). Three fractional distillations from an Arbuzov flask gave a colorless, oily liquid (5 g, 34.9%) with b.p. 128-130° (4.5 mm).

Reaction with triethyl phosphite. A mixture of 9.5 g of myrtenyl chloride and 10 g of triethyl phosphite in a sealed tube was heated for 10 hr at 130-155°. The first fractional distillation gave 9.8 g (65.5%) of a colorless, oily liquid with b.p. 117-118° (1 mm).

MR_D		Empirical formula	% P		% S	
found	calculated		found	calculated	found	calculated
63.67 63.57	63.93	$C_{12}H_{21}O_3P$	12.57, 12.38 12.03, 12.10	12.67	—	—
73.17 73.07	73.17	$C_{11}H_{25}O_3P$	11.14, 11.18 11.09, 10.96	11.37	—	—
82.91 82.88	82.41	$C_{16}H_{29}O_3P$	10.07, 10.11 10.19, 10.17	10.31	—	—
91.58 91.58	91.64	$C_{18}H_{33}O_3P$	9.42, 9.23 9.23, 9.20	9.43	—	—
82.55	82.23	$C_{14}H_{25}O_3PS$	10.21	10.17	10.92, 10.83	10.53
90.27	89.72	$C_{14}H_{25}O_2PS_2$	9.26	9.66	20.21	20.01

Reaction with tri-n-propyl phosphite. A mixture of 10 g of myrtenyl chloride and 13.5 g of tri-n-propyl phosphite in a sealed tube was heated for 32 hr at 135-160°. From the reaction products was isolated 12.8 g (72.7%) of colorless oil with b.p. 138-139° (1 mm).

Reaction with tri-n-butyl phosphite. A mixture of 10.2 g of myrtenyl chloride and 15 g of tri-n-butyl phosphite was heated in a sealed tube for 24 hr at 130-180°. The first fractional distillation gave 13.2 g (68.6%) of colorless oil with b.p. 166-167° (3 mm).

Reaction with sodium dimethylphosphite. The sodium compound was prepared from 6.6 g of dimethylphosphorous acid and 1.4 g of sodium in 100 ml of anhydrous benzene. The compound settled out on the walls of the flask during formation. Myrtenyl chloride (10 g) was added and the mixture refluxed with vigorous stirring for 8 hr. Fractional distillation of the reaction products led to isolation of only 1.1 g (7.6%) of oily liquid with b.p. 117° (2 mm).

Reaction with sodium diethylphosphite. To a solution of sodium diethylphosphite in benzene (prepared from 8 g of diethylphosphorous acid and 1 g of sodium in 90 ml of anhydrous benzene) was gradually added 10 g of myrtenyl chloride. Stirring and refluxing were continued for 5 hr, after which the precipitate was removed, the benzene taken off in vacuo on a water bath, and the residue distilled from an Arbuzov flask. Yield 9.8 g (61.4%) of colorless oil with b.p. 138° (4 mm). A test with CuI revealed the absence of trivalent phosphorus.

Reaction with sodium di-n-propylphosphite. To a solution of sodium di-n-propylphosphite [prepared from 9.3 g of di-n-propylphosphorous acid and 1.35 g Na in 135 ml gasoline (b.p. 90-110°)] was added 10.1 g myrtenyl chloride. The mixture was stirred at the boiling point of the gasoline for 9 hr. The precipitate could not be completely removed. The gasoline was taken off in vacuo on a water bath and the residue distilled three times to give 6 g (32.1%) of oil with b.p. 141° (2 mm). The product was odorless and colorless.

Reaction with sodium di-n-butylphosphite. To a solution of sodium di-n-butyl phosphite (11.4 g of di-n-butylphosphorous acid, 1.4 g of sodium and 100 ml of gasoline with b.p. 105-115°) was gradually added 10 g of myrtenyl chloride with heating and stirring. Heating was continued for 10 hr. The precipitate could not be separated. After the gasoline had been taken off, the gelatinous residue was treated with water and extracted with ether. The ethereal extract was dried with sodium sulfate and the ether removed. From the residue was isolated 13.1 g (68.1%) of product in the form of a slightly yellowish oil. Redistillations gave an oil with b.p. 165° (2.5 mm).

Reaction with sodium diethyl monothiophosphate. To a solution of sodium diethylmonothiophosphate in benzene (prepared from 8.2 g of diethylphosphorous acid, 1.5 g of sodium and 1.9 g of sulfur in 150 ml of anhydrous benzene) was gradually added 10 g of myrtenyl chloride. The mixture was heated for 12 hr at the boiling point of benzene. The colloidal precipitate could not be separated. After removal of the benzene, the residue distilled with decomposition. Repeated fractionation gave an orange liquid with the odor of burned onion (4.9 g or 27.4%); b.p. 165-166.5° (2.5 mm).

Reaction with sodium diethyldithiophosphate. To a solution of 11.6 g of sodium diethyldithiophosphate in 50 ml of acetone was gradually added 10 g of myrtenyl chloride with stirring, and the reaction mixture was heated on a water bath at 70° for 5 hr. The precipitated NaCl settled out overnight and was filtered off, the acetone was distilled, and the residue distilled from an Arbuzov flask to give a light-yellow, oily liquid with an unpleasant odor (12.2 g or 64.7%) with b.p. 159° (2.5 mm).

SUMMARY

1. Reaction of myrtenyl chloride with trialkyl phosphites and with sodium dialkylphosphites gave the corresponding dialkyl esters of myrtenylphosphinic acid.

2. Reaction of myrtenyl chloride with sodium diethylmonothio- and with diethyldithiophosphate gave the corresponding myrtenyldiethyl esters of monothio- and dithiophosphoric acid.

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•Original Russian pagination. See C. B. Translation.

INTERACTION OF COMPOUNDS OF TRIVALENT PHOSPHORUS WITH HALOGENATED ACID HALIDES

I. REACTION OF TRIALKYL PHOSPHITES WITH TRICHLOROACETYL CHLORIDE

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Reaction of trialkyl phosphites with acetyl chloride proceeds in accordance with the general scheme of the A. E. Arbuzov rearrangement and leads to formation of esters of acetylphosphinic acid [1]. However, an attempt [2] to prepare the dimethyl ester of trichloroacetylphosphinic acid by a similar route was unsuccessful: compound (I) was isolated, and the authors considered it to be formed by further transformations of the originally formed ester of trichloroacetylphosphinic acid.

$$(RO)_3P + CCl_3C(=O)Cl \xrightarrow{-RCl} \left[(RO)_2P(=O)-C(=O)-CCl_3\right] \xrightarrow[-RCl]{+(RO)_3P} \underset{(I)}{(RO)_2P(=O)-O-C(CCl_2=O)-P(OR)_2} \quad (1)$$

Triethyl phosphite was recently [3] reacted with trichloroacetylchloride and, in addition to (I), a substance was isolated to which the structure of a diketoester was attributed without adequate proof. The only evidence of this structure was the equimolar reaction of the substance with aqueous phenylhydrazine.

We undertook a more detailed study of the transformations taking place during reaction of phosphites with trichloroacetyl chloride, since the presence of a trichloromethyl radical at the carbonyl group could conceivably result (if only partially) in the following reaction course, with formation of previously known trichlorovinyl esters.

$$(RO)_3P + CCl_3C(=O)Cl \rightarrow (RO)_2P(=O)OCCl=CCl_2 + RCl \quad (2)$$

Reaction of trialkyl phosphites with trichloroacetyl chloride under mild conditions in presence of a considerable excess of trichloroacetyl chloride led to isolation, apart from (I), of compounds (15-25% yield) which were identified as trichlorovinyl dialkylphosphates. Molecular weight determinations and analytical data thus indicate the presence of only one phosphorus atom. A study of the structure of the compounds (Table 1) established that they add on two chlorine atoms with formation of pentachloro derivatives (Table 2), they are completely transformed into phosphoric (but not phosphorous•) acid on acid hydrolysis and the infrared spectrum exhibits an absorption band characterizing the C = C bond (1613 cm^{-1})•• (Fig. 1).

• As previously established, hydrolysis of esters of acetylphosphinic acid in an acid medium leads to phosphorous acid, whereas trialkyl phosphates are hydrolyzed to phosphoric acid [1].

•• It may therefore be suggested that the compound described as the diethyl ester of trichloroacetylphosphinic acid [3] is actually trichlorovinyl diethylphosphate.

TABLE 1

No.	Formula	Boiling point at 0.05 mm	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Yield (%)	Found (%) P	Found (%) Cl	Calculated (%) P	Calculated (%) Cl
1	$(CH_3O)_2POCCl{=}CCl_2$ ‖ O	75—76°	1.5145	1.4729	47.2	46.79	14.5	12.65, 12.50	40.5, 41.0	12.15	41.7
2	$(C_2H_5O)_2POCCl{=}CCl_2$ ‖ O	82—83	1.3850	1.4645	56.5	56.03	18.6	10.81	37.4, 37.3	10.95	37.5
3	$(C_3H_7O)_2POCCl{=}CCl_2$ ‖ O	100—101	1.2623	1.4615	65.6	65.27	35.2	10.32, 10.28	34.0, 34.2	10.0	34.3
4	$(C_4H_9O)_2POCCl{=}CCl_2$ ‖ O	120—124	1.2200	1.4605	74.8	74.50	20.6	9.67, 9.77	30.6, 30.8	9.2	31.5
5	$(C_2H_5O)_2POC{-}P(OC_2H_5)_2$ ‖ ‖ ‖ O CCl_2 O	130—131	1.3380	1.4690	80.2	80.5	67.3	15.95, 15.80	18.2, 18.15	16.1	18.4

TABLE 2

No.	Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Found (%) P	Found (%) Cl	Calculated (%) P	Calculated (%) Cl
1	$(CH_3O)_2POCCl_2CCl_3$ ‖ O	106—108°(10^{-3})	1.6020	1.4780	57.6	57.0	— —	54.0, 53.8	—	54.3
2	$(C_2H_5O)_2POCCl_2CCl_3$ ‖ O	120—121 ($1.64 \cdot 10^{-4}$)	1.5045	1.4770	66.5	66.23	8.72, 7.86	50.2, 50.4	8.75	50.1
3	$(C_3H_7O)_2POCCl_2CCl_3$ ‖ O	160—164 ($1.64 \cdot 10^{-4}$)	1.4199	1.4770	76.2	75.5	8.08, 7.99	46.1, 45.6	8.1	46.4

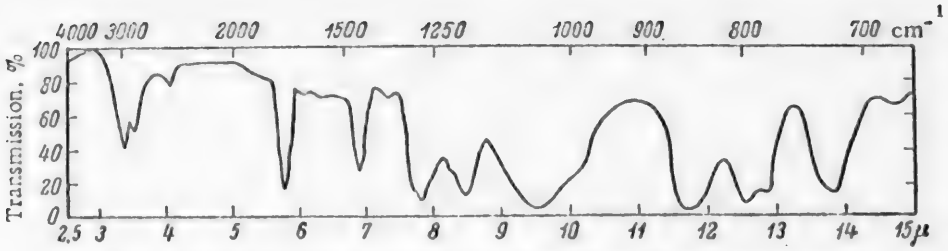

Fig. 1. Infrared absorption spectrum of trichlorovinyl diethylphosphate.

TABLE 3

No.	Formula	Boiling point at 0.05 mm	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Yield (%)	Found (%) P	Found (%) Cl	Calculated (%) P	Calculated (%) Cl
1	$(CH_3O)_2P(O)-C(O)-CCl_3$	85—86°	1.5300	1.4740	46.7	46.2	41	12.01, 12.45	41.2, 41.4	12.15	41.7
2	$(C_2H_5O)_2P(O)-C(O)-CCl_3$	95—97	1.4100	1.4655	55.5	55.4	32.5	10.83, 10.94	37.2, 36.8	10.92	37.5

Formation of β,β-dichloro-α-dialkylphosphonovinyl dialkylphosphate (I) is very probably the consequence of further transformations of α,β,β-trichlorovinyl dialkylphosphate since the latter, as experimentally established, enters into reaction with trialkyl phosphites to give (I). The reaction evidently involves the chlorine atom in the α-position.•

$$(RO)_2POC(O)-CCl_2Cl + (RO)_3P \longrightarrow (RO)_2POC(O)-CCl_2-P(O)(OR)_2 + RCl \qquad (3)$$

It is interesting to note that the latter reaction is one of the few examples of the Arbuzov rearrangement with participation of a halovinyl group.

With the objective of comparing the properties of the prepared trichlorovinyl dialkylphosphates with those of the isomeric esters of trichloroacetylphosphinic acid, the latter were synthesized by reaction of trichloroacetyl chloride with dialkyl phosphites (Table 3).

$$(RO)_2P(O)H + CCl_3C(O)Cl \longrightarrow (RO)_2P(O)-C(O)-CCl_3 + HCl \qquad (4)$$

The constants of these compounds differ little from those of the corresponding trichlorovinyl dialkylphosphates; however, unlike the latter, the esters of trichloroacetylphosphinic acid undergo acid hydrolysis with formation of phosphoric acid, and the infrared spectrum contains the band characterizing the C = O group(1724 cm^{-1}) (Fig. 2).

It was shown that esters of trichloroacetylphosphinic acid react with trialkylphosphites with formation of β,β-dichloro-α-dialkylphosphinovinyl dialkylphosphates, as suggested by Kabachnik and Rossiiskaya [see scheme (1)]. For example, the reaction of trimethyl phosphite with the dimethyl ester of trichloroacetylphosphinic acid gave β,β-dichloro-α,α-dimethylphosphonovinyl dimethylphosphate with constants and analytical data identical

• Under mild hydrolysis conditions, trichlorovinyl esters split of only one chlorine atom, presumably from the α-position since the latter must be more labile (closer to the positively charged phosphorus).

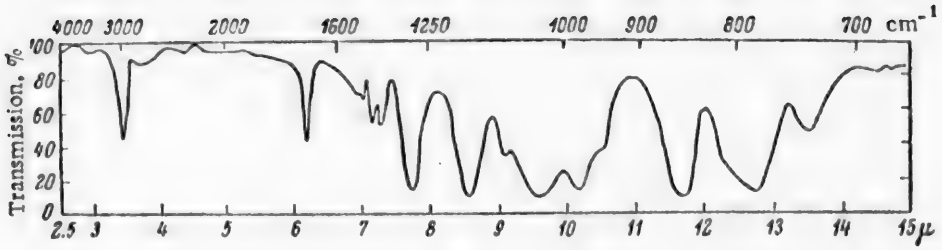

Fig. 2. Infrared spectrum of the dimethyl ester of trichloroacetylphosphinic acid.

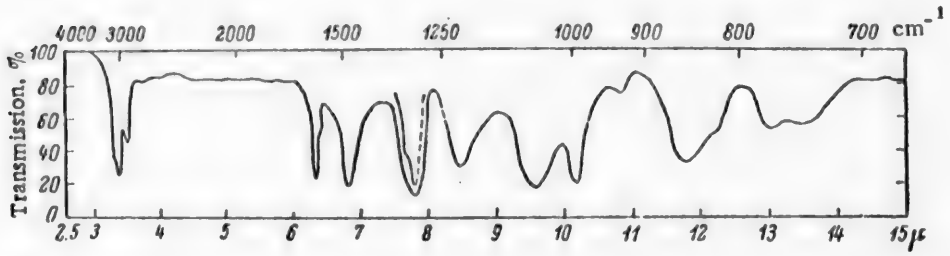

Fig. 3. Infrared absorption spectrum of β,β-dichloro-α-dimethylphosphonovinyl dimethylphosphate.

with those for the substance described by Kabachnik and Rossiiskaya [2]. The structure of the product was also confirmed by the infrared spectrum whose absorption band at 1582 cm^{-1} is characteristic of the C = C valence vibration (Fig. 3).

It has thus been experimentally established that formation of β,β-dichloro-α-dialkylphosphonovinyl dialkylphosphate can actually proceed by scheme (1) as well as by scheme (3). Scheme (3), however, is more probable since esters of trichloroacetylphosphinic acid are not isolated when trichloroacetyl chloride reacts with trialkyl phosphates.

EXPERIMENTAL

1. Reaction of trialkyl phosphites with trichloroacetyl chloride (Table 1). Into a three-necked flask, fitted with stirrer, dropping funnel, nitrogen inlet tube and reflux condenser, was charged 1 mole of trichloroacetyl chloride which had been freshly distilled in vacuo. In a nitrogen atmosphere gradual addition was then made with stirring of 0.15 mole of trialkyl phosphite* and 300 ml of dry ether at room temperature. The next day the solvent and excess of trichloroacetyl chloride were removed and the residue distilled in vacuo. Several distillations gave a 15-25% yield of α,β,β-trichlorovinyl dialkylphosphate. When triethyl phosphite was brought into reaction, an additional product was β,β-dichloro-α,α-dialkylphosphonovinyl diethylphosphate.

2. Pentachloroethyl dialkylphosphates (Table 2). Dry carbon tetrachloride (50-70 ml) in a quartz flask was saturated with chlorine. Addition was then made of 3-4 g of trichlorovinyl dialkylphosphate and the mixture irradiated with ultraviolet light for an hour. The temperature rose spontaneously to 30-35° within 5-10 min after the start of irradiation. After the irradiation, the solvent and chlorine were taken off and the residual colorless oil distilled in vacuo. Pentachloroethyl dialkylphosphates are colorless, transparent, poorly mobile liquids.

3. β,β-Dichloro-α-dimethylphosphonovinyl dimethylphosphate. a) A mixture of 1.2 g of trimethyl phosphite (0.01 mole) and 2.3 g of trichlorovinyl dimethylphosphate (0.01 mole) was heated at 100° for 3 hr. Yield 2.1 g (64%).

B.p. 126° (0.05 mm), d_4^{20} 1.4900, nD^{20} 1.4707.

b) To 5.1 g (0.02 mole) of dimethyl ester of trichloroacetylphosphinic acid in 20 ml of ether was added 2.48 g (0.02 mole) of trimethyl phosphite dissolved in 10 ml of ether. The next day the reaction mixture was distilled. Yield 5.0 g (76%).

* The trialkyl phosphites were previously distilled over sodium for elimination of any traces of dialkyl phosphites.

B.p. 127-128° (0.05 mm), d_4^{20} 1.4885, nD^{20} 1.4760.

After hydrolysis in hydrochloric acid, the determination of the content of phosphorus in the form of phosphorous acid gave 9.39%, and when in the form of phosphoric acid gave 9.32% (the calculated content was 9.43%).

4. Esters of trichloroacetylphosphinic acid (Table 3). A solution of 0.2 mole of dialkyl phosphite in 100 ml of dry benzene was placed in a flask. A solution of 0.2 mole of trichloroacetyl chloride in 50 ml of benzene was added in a nitrogen stream in a vacuum of 50-60 mm. The benzene and hydrogen chloride were then eliminated in vacuo and the residue distilled. Yield 30-40%. Esters of trichloroacetylphosphinic acid are poorly mobile liquids, soluble in common organic solvents.

SUMMARY

1. Reaction of trialkyl phosphites with trichloroacetyl chloride gave a new group of compounds – the trichlorovinyl dialkylphosphates.

2. Chlorination of trichlorovinyl dialkylphosphates gave the corresponding pentachloroethyl dialkylphosphate

3. It was shown that trichlorovinyl dialkylphosphates enter into a reaction with trialkyl phosphites of the Arbuzov-rearrangement type with formation of β,β-dichloro-α-dialkylphosphonovinyl dialkylphosphates.

4. Esters of trichloroacetylphosphinic acid were prepared by reaction of dialkyl phosphites with trichloroacetyl chloride.

5. It was shown that esters of trichloroacetylphosphinic acid react with trialkyl phosphites to form β,β-dichloro-α-dialkylphosphonovinyl dialkylphosphates.

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*Original Russian pagination. See C. B. Translation.

REACTION OF β-CHLOROETHYL CHLOROSULFONATE WITH ESTERS OF ACIDS OF PHOSPHORUS

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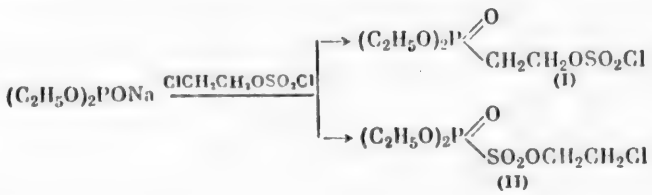
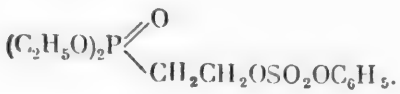
Halogenated esters of chlorosulfonic acid are known to be powerful bactericides [1]. Reactions of these compounds with derivatives of phosphoric acid have not been described in the literature. It was therefore of interest to study the reaction of β-chloroethyl chlorosulfonate with sodium salts of phosphorous and thio- and dithiophosphoric acids. Salts of these acids, for example sodium diethylphosphite, can react in two directions:



We isolated the diethyl ester of β-chlorosulfoethylphosphinic acid (I). Its structure was confirmed by study of its reaction with sodium phenoxide and diethylamine, as well of the reaction of diethyl phosphite with ethyl chlorosulfonate not containing a halogen in the ethyl radical.

Ethyl chlorosulfonate, containing the SO_2Cl group, does not form a compound of the composition $(C_2H_5O)_2P(O)SO_2OC_2H_5$ with sodium diethylphosphite. The main products of the reaction are diethylphosphorous acid, SO_3 and HCl, i.e., the normal process of breakdown of ethyl chlorosulfonate [2] predominates. β-Chloroethyl chlorosulfonate also breaks down slowly, particularly when heated [3]. This is evidently the cause of the low yields of the products obtained.

The reaction with sodium phenoxide takes place in the cold. Saponification with alcoholic alkali of the product of reaction with the phenoxide gives phenol and sodium sulfate. Consequently the phenyl ester of (I) (not isolated in the pure form) has the structure:



Compound (I) reacts with facility with diethylamine in the cold, indicating that chlorine is present in the acid chloride form in the terminal SO_2Cl group. It was also prepared by Arbuzov isomerization from triethyl phosphite and β-chloroethyl chlorosulfonate. In both cases the product contained a pentavalent phosphorus atom (no decolorization of bromine water and no reaction with cuprous chloride and sulfur).

Compounds of the following types were obtained in this investigation:

1. $(RO)_2P(=O)CH_2CH_2OSO_2Cl$ (R = C_2H_5, n-C_3H_7, iso-C_3H_7).

2. $(RO)_2P(=S)OCH_2CH_2OSO_2Cl$ (R = C_2H_5, n-C_3H_7).

3. $(H_5C_2O)_2P(=S)SCH_2CH_2OSO_2Cl$.

EXPERIMENTAL

Reaction of sodium diethylphosphite with β-chloroethyl chlorosulfonate. β-Chloroethyl chlorosulfonate was prepared by condensation of sulfuryl chloride with ethylene oxide [4].

Sodium diethylphosphite was prepared from 13.8 g of diethylphosphorous acid and 2.3 g of metallic sodium. To the cooled sodium salt was added 17.8 g of β-chloroethyl chlorosulfonate. The mixture was heated for 2 hr on a water bath, cooled and treated with iced water. The ethereal layer was collected, dried with anhydrous sodium sulfate and fractionated in vacuo. Yield 10.2 g (44.3%). The ester is a colorless oil with a characteristic unpleasant odor, insoluble in water and readily soluble in organic solvents.

B.p. 120-121° (4 mm), nD^{20} 1.4095, d_4^{20} 1.1047.

Found %: P 11.25; 11.16; Cl 12.80. $C_6H_{14}O_6PSCl$. Calculated %: P 11.03; Cl 12.69.

Reaction of sodium diethylphosphite with ethyl chlorosulfonate. To the sodium diethylphosphite prepared from 27.6 g (0.2 mole) of diethylphosphorous acid was added 29.6 g (0.2 mole) of ethyl chlorosulfonate. The mixture was heated on a water bath for 2 hr. The liberated gases were passed through alkali solution and then through bromine water. The sodium chloride was removed and the ether distilled off. There was obtained 21.3 g (74.4%) of product. B.p. 95-96° (24 mm) and 186° (760 mm); nD^{20} 1.4030. These data agree with those in the literature for diethylphosphorous acid [5].

Reactions of the diethyl ester of β-chlorosulfoethylphosphinic acid. a) With diethylamine. To 2.8 g of the ester in absolute ether was added 1.46 g of diethylamine. Diethylamine hydrochloride came down after 1-2 min (0.97 g or 89%). The ether was removed to leave 2.98 g of oil (90.4%) that did not distil in an ordinary vacuum.

Found %: P 10.51, 10.03. $C_4H_{24}O_6NPS$. Calculated %: P 9.77.

b) With sodium phenoxide. To an ethereal solution of 0.942 g of sodium phenoxide was added 2.08 g of the ester. There was obtained 2.21 g of oily product which was saponified with alcoholic alkali. Phenol and sodium sulfate were found in the products of saponification.

Reaction of triethyl phosphite with β-chloroethyl chlorosulfonate (Arbuzov rearrangement). Reaction was effected in an Arbuzov flask with 16.62 g of triethyl phosphite and 17.9 g of β-chloroethyl chlorosulfonate by the usual procedure. A fraction with a weight of 9.21 g (31.9%) was isolated.

B.p. 117-118° (2 mm); nD^{20} 1.4087, d_4^{20} 1.1044.

Found %: P 10.79; Cl 12.45. $C_6H_{14}O_6PSCl$. Calculated %: P 11.03; Cl 12.69.

O,O-Di-n-propyl-O-chlorosulfoethylphosphinic acid. Prepared from 8.3 g of di-n-propylphosphorous acid 1.15 g of sodium and 8.95 g of β-chloroethyl chlorosulfonate. Yield 3.6 g (25.5%).

B.p. 133-134° (2 mm), nD^{20} 1.4225, d_4^{20} 1.0574.

Found %: P 10.52; 10.31. $C_8H_{16}O_6PSCl$. Calculated %: P 10.01.

O,O-Di-isopropyl-O-β-chlorosulfoethylphosphinic acid. From 8.3 g of diisopropylphosphorous acid, 1.15 g of sodium and 8.95 g of chlorosulfonate. Yield 4.1 g (26.61%).

B.p. 63-64° (1 mm), nD^{20} 1.4195, d_4^{20} 1.0685.

Found %: P 10.92; 9.85. $C_8H_{16}O_6PSCl$. Calculated %: P 10.01.

O,O-Diethyl-O-β-chlorosulfoethylthiophosphate. Prepared from 13.8 g of diethylphosphorous acid, 2.3 g of sodium, 3.2 g of sulfur and 17.8 g of β-chloroethyl chlorosulfonate in a medium of gasoline.

After the mixture had been heated for 3 hr, the gasoline was removed and the residue fractionated in vacuo. Yield 11.81 g (37.78%).

B.p. 112° (4 mm), nD^{20} 1.4495, d_4^{20} 1.0632.

Found %: P 10.2; Cl 13.50. $C_6H_{14}O_5PS_2Cl$. Calculated %: P 9.93; Cl 13.01.

O,O-Dipropyl-O-β-chlorosulfoethylthiophosphate. Prepared under similar conditions from 16.6 g of dipropylphosphorous acid, 2.3 g of sodium, 3.2 g of sulfur and 17.8 g of β-chloroethyl chlorosulfonate. Yield 9.1 g (26.87%).

B.p. 120-121° at 7 mm; nD^{20} 1.4770, d_4^{20} 1.0028.

Found %: P 9.10, 8.85. $C_8H_{16}O_5PS_2Cl$. Calculated %: P 9.16.

The derivatives of thiophosphoric acid are light-yellow, oily liquids with a strong and unpleasant odor.

O,O-Diethyl-S-β-chlorosulfoethyldithiophosphate is a light-yellow oil, readily soluble in ether, benzene and acetone, insoluble in water. Prepared from 18.6 g of diethyldithiophosphoric acid (b.p. 90-92° at 8 mm) [6], 10.6 g of anhydrous sodium carbonate and 17.9 g of β-chloroethyl chlorosulfonate. Yield 5.06 g.

B.p. 84-85° at 7 mm, nD^{20} 1.4995, d_4^{20} 1.3652.

Found %: P 9.08, 9.26. $C_6H_{14}O_5PS_3Cl$. Calculated %: P 9.42.

SUMMARY

1. The reaction of β-chloroethyl chlorosulfonate with diethyl-, dipropyl and diisopropylphosphites, diethyl- and dipropylthiophosphates and diethyldithiophosphoric acid was studied.

2. It was established that β-chloroethyl chlorosulfonate reacts in these reactions at the $ClCH_2CH_2$ group and not at the SO_2Cl group.

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THE ADDITION OF TRICHLOROSILANE TO DIALKYL(PHENYL, CHLORO)DIALLYLSILANES

SOME SILICOHYDROCARBONS OBTAINED ON THE BASIS OF THE ADDITION PRODUCTS

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In the preceding communication we described reactions of addition of trichlorosilane to trialkyl(phenyl, chloro)allylsilanes, as well as some silicohydrocarbons obtained on the basis of the addition products. Kanazashi [2] demonstrated the possibility of addition of trichlorosilane to dialkyldivinylsilanes at the two double bonds of the vinyl radicals.

$$R_2Si\begin{matrix}CH{=}CH_2\\CH{=}CH_2\end{matrix} + HSiCl_3 \rightarrow R_2Si\begin{matrix}CH_2CH_2SiCl_3\\CH_2CH_2SiCl_3\end{matrix}$$

In the present communication we describe a study of the addition of trichlorosilane to diallyl derivatives of silicon. The activity of benzoyl peroxide, platinum on carbon, and chloroplatinic acid as catalysts for the addition reaction was studied.

Comparison of the yields of addition products (see Tables 2 and 3) reveals that chloroplatinic acid and platinum on carbon are more active than benzoyl peroxide as catalysts in the addition of trichlorosilane to dialkyl-(phenyl, chloro)diallylsilanes. A study of the addition of trichlorosilane to diallyl derivatives of silicon revealed the same regularities that were noted previously for reactions of trichlorosilane with monoallyl derivatives of silicon [3]. The activity of the double bond in dialkyl(phenyl, chloro)diallylsilanes increases both with increasing size of alkyl radicals and with their replacement by phenyl radicals or chlorine atoms.

Table 4 gives the physicochemical properties of silicohydrocarbons synthesized by reaction of alkyllithiums and phenyllithium with chloro derivatives obtained by addition of trichlorosilane to dialkyl(phenyl, chloro)diallylsilanes at the two double bonds.

The infrared spectra of these silicohydrocarbons showed that addition of trichlorosilane to diallyl derivatives of silicon in presence of benzoyl peroxide, platinum on carbon and chloroplatinic acid does not proceed in accordance with the Markovnikov rule.

$$R_2Si\begin{matrix}CH_2CH{=}CH_2\\CH_2CH{=}CH_2\end{matrix} + 2HSiCl_3 \rightarrow Cl_3SiCH_2CH_2CH_2Si(R)CH_2CH{=}CH_2 + Cl_3SiCH_2CH_2CH_2Si(R)CH_2CH_2CH_2SiCl_3$$

R = CH_3, C_2H_5, C_3H_7, C_4H_9, C_6H_5, Cl.

TABLE 1

Serial No.	Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Yield (in %)
1	$(CH_3)_2Si(CH_2CH=CH_2)_2$	135—136.5°(751)	1.4445	0.7672	48.22	48.16	64.3
2	$(C_2H_5)_2Si(CH_2CH=CH_2)_2$	95—97 (33)	1.4590	0.8068	57.24	57.06	70.4
3	$(C_3H_7)_2Si(CH_2CH=CH_2)_2$	76—78 (2)	1.4555	0.8050	66.74	66.24	72.3
4	$(C_4H_9)_2Si(CH_2CH=CH_2)_2$	86—88 (2)	1.4610	0.8130	75.84	75.73	87.0
5	$(C_6H_5)_2Si(CH_2CH=CH_2)_2$	140—142 (2)	1.5754	0.9948	87.86	87.86	76.7
6	$(CH_3)C_6H_5Si(CH_2CH=CH_2)_2$	239—241 (752)	1.5220	0.9090	68.04	67.88	74.2
7	$Cl_2Si(CH_2CH=CH_2)_2$	166—168 (748)	—	—	—	—	42.0

TABLE 2

Serial No.	Compound	Boiling point (pressure in mm)	% Cl found	% Cl calculated	Yield (in %) catalyst: benzoyl peroxide	catalyst: chloroplatinic acid	catalyst: platinum on carbon
1	$(CH_3)_2(CH_2=CHCH_2)SiCH_2CH_2CH_2SiCl_3$	115—118°(7)	38.41, 38.50	38.66	—	28.5	20.2
2	$(C_2H_5)_2(CH_2=CHCH_2)SiCH_2CH_2CH_2SiCl_3$	124—126 (4)	34.80, 34.72	35.05	—	29.0	25.7
3	$(C_3H_7)_2(CH_2=CHCH_2)SiCH_2CH_2CH_2SiCl_3$	167—169 (9)	32.70, 32.90	32.84	5.1	29.7	25.5
4	$(C_4H_9)_2(CH_2=CHCH_2)SiCH_2CH_2CH_2SiCl_3$	186—189 (9)	26.82, 26.91	27.04	18.2	28.8	26.6
5	$(C_6H_5)_2(CH_2=CHCH_2)SiCH_2CH_2CH_2SiCl_3$	222—224 (4)	26.20, 26.37	26.65	20.0	17.6	—*
6	$C_6H_5(CH_3)(CH_2=CHCH_2)SiCH_2CH_2CH_2SiCl_3$	180—182 (5)	31.67, 31.80	31.52	17.3	13.8	—*
7	$Cl_2(CH_2=CHCH_2)SiCH_2CH_2CH_2SiCl_3$	153—156 (4)	38.55, 38.48	38.61	52.8	8.3	—*

* Addition of trichlorosilane to diphenyl-, methylphenyl- and dichlorodiallylsilanes was not performed in presence of platinum on carbon.

TABLE 3

Serial No.	Compound	Boiling point (pressure in mm)	% Cl		Yield (%)		
			found	calculated	catalyst: benzoyl peroxide	catalyst: chloroplatinic acid	catalyst: platinized carbon
1	$(CH_3)_2Si(CH_2CH_2CH_2SiCl_3)_2$	163—165°(5)	51.93, 52.13	51.77	--	27.9	36.3
2	$(C_2H_5)_2Si(CH_2CH_2CH_2SiCl_3)_2$	176—178 (5)	48.49, 48.83	48.47	—	32.0	32.10
3	$(C_3H_7)_2Si(CH_2CH_2CH_2SiCl_3)_2$	193—195 (5)	45.79, 45.47	45.56	--	32.6	33.8
4	$(C_4H_9)_2Si(CH_2CH_2CH_2SiCl_3)_2$	219—221 (5)	42.49, 42.82	42.98	—	34.1	37.4
5	$(C_6H_5)_2Si(CH_2CH_2CH_2SiCl_3)_2$	268—270 (4)	39.73, 39.68	39.77	7.7	52.4	*
6	$C_6H_5(CH_3)Si(CH_2CH_2CH_2SiCl_3)_2$	212—214 (5)	44.74, 44.60	44.97	6.1	41.4	*
7	$Cl_2Si(CH_2CH_2CH_2SiCl_3)_2$	210—212 (2)	62.40, 62.51	62.77	11.2	67.3	*

TABLE 4

Serial No.	Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Found (%) C	Found (%) H	Calculated (%) C	Calculated (%) H
1	$(CH_3)_2Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	136—138°(6)	1.4448	0.8005	95.90	95.84	58.10, 58.18	12.53, 12.55	58.25	12.57
2	$(C_2H_5)_2Si[CH_2CH_2CH_2Si(C_2H_5)_3]_2$	224—226 (7)	1.4707	0.8500	131.75	131.92	66.66, 66.04	12.95, 12.93	65.92	13.07
3	$(C_3H_7)_2Si[CH_2CH_2CH_2Si(C_3H_7)_3]_2$	242—244 (6)	1.4687	0.8422	169.56	169.92	70.31, 70.18	13.36, 13.21	70.23	13.36
4	$(C_4H_9)_2Si[CH_2CH_2CH_2Si(C_4H_9)_3]_2$	273—275 (5)	1.4702	0.8450	206.31	206.32	73.11, 73.22	13.52, 13.44	72.99	13.54
5	$(C_6H_5)_2Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$	M. p. 114.5—116	—	—	—	—	82.76, 82.92	6.86, 6.80	82.60	6.67
6	$(CH_3)_2Si[CH_2CH_2CH_2Si(C_2H_5)_3]_2$	213—215 (7.5)	1.4678	0.8440	122.70	122.90	64.56, 64.61	13.01, 13.01	64.44	12.98
7	$(CH_3)_2Si[CH_2CH_2CH_2Si(C_3H_7)_3]_2$	236—238 (7)	1.4665	0.8400	150.78	151.40	68.26, 68.30	13.30, 13.28	68.34	13.23
8	$(CH_3)_2Si[CH_2CH_2CH_2Si(C_4H_9)_3]_2$	264—265 (8)	1.4680	0.8429	178.44	178.70	70.77, 70.81	13.62, 13.60	71.03	13.41
9	$(CH_3)_2Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$	M. p. 91—93	—	—	—	—	79.89, 79.78	7.38, 7.26	79.45	7.32
10	$CH_3(C_6H_5)Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	188—190 (5)	1.4840	0.8672	115.47	115.60	65.18, 65.20	10.89, 10.80	65.13	10.90
11	$CH_3(C_6H_5)Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$	M. p. 103—104	—	—	—	—	81.29, 81.27	6.98, 7.01	81.38	6.97
12	$(C_6H_5)_2Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	217—219 (5)	1.5218	0.9310	135.20	135.48	69.70, 69.73	9.63, 9.78	69.83	9.76

* Addition of trichlorosilane to diphenyl-, methylphenyl- and dichlorodiallylsilanes was not carried out in presence of platinized carbon.

EXPERIMENTAL

I. Preparation of Dialkyl(phenyl, chloro)diallylsilanes

These were prepared by the Grignard reaction and their properties agreed with those in the literature (see Table 1).

1. Dimethyldiallylsilane. From 60 g of magnesium, 280 g (2.31 moles) of allyl bromide and 129 g (1 mole) of dimethyldichlorosilane was obtained 90 g (64.3%).

2. Diethyldiallylsilane. From 72 g of magnesium, 300 g (2.48 moles) of allyl bromide and 157 g (1 mole) of diethyldichlorosilane was obtained 118.3 g (70.4%).

3. Dipropyldiallylsilane. From 45 g of magnesium, 150 g (1.24 moles) of allyl bromide and 83 g (0.45 mole) of dipropyldichlorosilane was obtained 68 g (72.3%).

4. Dibutyldiallylsilane. From 46 g of magnesium, 150 g (1.24 moles) of allyl bromide and 80 g (0.37 mole) of dibutyldichlorosilane was obtained 74.0 g (87%).

5. Diphenyldiallylsilane. From 35 g of magnesium, 130 g (1.07 moles) of allyl bromide and 95 g (0.375 mole) of diphenyldichlorosilane was obtained 76 g (76.7%).

6. Methylphenyldiallylsilane. From 80 g of magnesium, 280 g (2.32 moles) of allyl bromide and 191 g (1 mole) of methylphenyldichlorosilane was obtained.150 g (74.2%).

7. Dichlorodiallylsilane. From 60 g of magnesium, 270 g (2.23 moles) of allyl bromide and 170 g (1 mole) of silicon tetrachloride was obtained 76 g (42%).

Found %: Cl 39.0, 39.20. $C_6H_{10}SiCl_2$. Calculated %: Cl 39.22.

II. Addition of Trichlorosilane to Dialkyl(phenyl, chloro)diallylsilanes (Tables 2 and 3)

The diallyl derivative of silicon and the catalyst were charged into a three-necked flask equipped with stirrer, reflux condenser and dropping funnel. Trichlorosilane was slowly stirred in. The catalysts were benzoyl peroxide, platinum on carbon (16% Pt by weight) and chloroplatinic acid (0.1 molar solution of $H_2PtCl_6 \cdot 6H_2O$ in isopropyl alcohol). In presence of benzoyl peroxide heating was carried out for 25 hr at 45-65°; in presence of $H_2PtCl_6 \cdot 6H_2O$ at 50° for 10 hr and then at 80° for 2 hr. Experiments with platinized carbon were run in a 0.8-liter steel autoclave at 190-210° and 10 atm for 20 hr. Fractionation gave products of addition of trichlorosilane both at one and at two double bonds with the dialkyl derivatives of silicon.

1. Addition of trichlorosilane to dimethyldiallylsilane. a) A mixture of 42 g (0.3 mole) of dimethyldiallylsilane, 108.5 g (0.8 mole) of trichlorosilane and 5 g of benzoyl peroxide was heated at 45-65° for 25 hr. Substantially no addition product was obtained.

b) A mixture of 50 g (0.36 mole) of dimethyldiallylsilane, 200 g (1.47 moles) of trichlorosilane and 0.5 g of platinized carbon was heated in an autoclave at 190-200° and 10 atm for 20 hr. Products were 19.8 g (20.2%) of dimethylallyl-(trichlorosilylpropyl)silane and 53.1 g (36.3%) of dimethyldi(trichlorosilylpropyl)silane.

c) From 42 g (0.3 mole) of dimethyldiallylsilane and 95 g (0.7 mole) of trichlorosilane in presence of 1 ml of chloroplatinic acid solution was obtained 23.8 g (28.5%) of dimethylallyl(trichlorosilylpropyl)silane and 34.5 g (27.9%) of dimethyldi(trichlorosilylpropyl)silane.

2. Addition of trichlorosilane to diethyldiallylsilane. a) A mixture of 42 g (0.25 mole) of diethyldiallylsilane, 95 g (0.7 mole) of trichlorosilane and 5 g of benzoyl peroxide was heated at 40-70° for 25 hr. Fractional distillation gave only traces of addition products.

b) A mixture of 52 g (0.3 mole) of diethyldiallylsilane, 200 g (1.47 mole) of trichlorosilane and 0.5 g of platinized carbon was heated in an autoclave at 190-200° and 10 atm for 20 hr. Products were 23.1 (25%) of diethylallyl(trichlorosilylpropyl)silane and 43.7 g (32.1%) of diethyldi(trichlorosilylpropyl)silane.

c) From 42 g (0.25 mole) of diethylallylsilane and 82 g (0.6 mole) of trichlorosilane in presence of 1 ml of chloroplatinic acid solution were obtained 22 g (29%) of diethylallyl(trichlorosilylpropyl)silane and 33.1 g (30.2%) of diethyldi(trichlorosilylpropyl)silane.

3. Addition of trichlorosilane to dipropyldiallylsilane. a) From 39 g (0.2 mole) of dipropyldiallylsilane, 82 g (0.6 mole) of trichlorosilane and 5 g of benzoyl peroxide was obtained 3.4 g (5.1%) of dipropylallyl(trichlorosilylpropyl)silane.

b) A mixture of 49 g (0.25 mole) of dipropyldiallylsilane, 162 g (1.2 mole) of trichlorosilane and 0.5 g of platinized carbon was heated in an autoclave at 200-210° and 10 atm for 20 hr. Products were 21.1 g (25.5%) of dipropylallyl(trichlorosilylpropyl)silane and 39.4 g (33.8%) of dipropyldi(trichlorosilylpropyl)silane.

c) From 39 g (0.2 mole) of dipropyldiallylsilane and 82 g (0.6 mole) of trichlorosilane in presence of 1 ml of chloroplatinic acid solution were obtained 19.7 g (29.7%) of dipropylallyl(trichlorosilylpropyl)silane and 30.4 g (32.6%) of dipropyldi(trichlorosilylpropyl)silane.

4. Addition of trichlorosilane to dibutyldiallylsilane. a) From 33.6 g (0.15 mole) of dibutyldiallylsilane, 61 g (0.45 mole) of trichlorosilane and 5 g of benzoyl peroxide was obtained 9.8 g (18.2%) of dibutylallyl(trichlorosilylpropyl)silane.

b) A mixture of 60 g (0.27 mole) of dibutyldiallylsilane, 200 g (1.47 g moles) of trichlorosilane and 0.5 g of platinized carbon was heated in an autoclave at 200-210° and 10 atm for 20 hr. Products were 25.5 g (26.6%) of dibutylallyl(trichlorosilylpropyl)silane and 49.4 g (37.4%) of dibutyldi(trichlorosilylpropyl)silane.

c) From 45 g (0.2 mole) of dibutyldiallylsilane and 82 g (0.6 mole) of trichlorosilane in presence of 1 ml of chloroplatinic acid solution were obtained 20.7 g (28.8%) of dibutylallyl(trichlorosilylpropyl)silane and 33.7 g (34.1%) of dibutyldi(trichlorosilylpropyl)silane.

5. Addition of trichlorosilane to diphenyldiallylsilane. a) From 40 g (0.15 mole) of diphenyldiallylsilane, 68 g (0.5 mole) of trichlorosilane and 5 g of benzoyl peroxide were obtained 12 g (20%) of diphenylallyl(trichlorosilylpropyl)silane and 6.2 g (7.7%) of diphenyldi(trichlorosilylpropyl)silane.

b) From 40 g (0.15 mole) of diphenyldiallylsilane and 68 g (0.5 mole) of trichlorosilane in presence of 1 ml of chloroplatinic acid solution were obtained 10.6 g (17.6%) of diphenylallyl(trichlorosilylpropyl)silane and 42.3 g (52.4%) of diphenyldi(trichlorosilylpropyl)silane.

6. Addition of trichlorosilane to phenylmethyldiallylsilane. a) From 40 g (0.2 mole) of phenylmethyldiallylsilane, 82 g (0.6 mole) of trichlorosilane and 5 g of benzoyl peroxide were obtained 11.6 g (17.3%) of phenylmethylallyl(trichlorosilylpropyl)silane and 5.8 g (6.1%) of phenylmethyldi(trichlorosilylpropyl)silane.

b) From 42 g (0.2 mole) of phenylmethyldiallylsilane and 82 g (0.6 mole) of trichlorosilane in presence of 1 ml of chloroplatinic acid solution were obtained 9.7 g (13.8%) of phenylmethylallyl(trichlorosilylpropyl)silane and 40.7 g (41.4%) of phenylmethyldi(trichlorosilylpropyl)silane.

7. Addition of trichlorosilane to dichlorodiallylsilane. a) From 36 g (0.2 mole) of dichlorodiallylsilane, 82 g (0.6 mole) of trichlorosilane and 5 g of benzoyl peroxide were obtained 33.4 g (52.8%) of dichloroallyl(trichlorosilylpropyl)silane and 101 g (11.2%) of dichlorodi(trichlorosilylpropyl)silane.

b) From 36 g (0.2 mole) of dichlorodiallylsilane and 82 g (0.6 mole) of trichlorosilane in presence of 1 ml of chloroplatinic acid solution were obtained 5.2 g (8.3%) of dichloroallyl(trichlorosilylpropyl)silane.

III. Preparation of Silicohydrocarbons on the Basis of Products of Addition of Trichlorosilane to Dialkyl(phenyl)diallylsilanes at Two Double Bonds (Table 4)

1. Dimethyldi(trimethylsilylpropyl)silane. From 15.7 g of lithium, 160 g (1.12 moles) of methyl iodide and 31 g (0.075 mole) of dimethyldi(trichlorosilylpropyl)silane was obtained 16.3 g (75.4%).

2. Diethyl(triethylsilylpropyl)silane. From 14 g of lithium, 111.2 g (1.02 moles) of ethyl bromide and 30 g (0.068 mole) of diethyldi(trichlorosilylpropyl)silane was obtained 19.6 g (72%).

3. Dipropyldi(tripropylsilypropyl)silane. From 6.5 g of lithium, 57.2 g (0.465 mole) of propyl bromide and 15.5 g (0.031 mole) of dipropyldi(trichlorosilylpropyl)silane was obtained 8.4 g (52.8%).

4. Dibutyldi(tributylsilylpropyl)silane. From 5.2 g of lithium, 51.5 g (0.375 mole) of butyl bromide and 12.3 g (0.025 mole) of dibutyldi-(trichlorosilylpropyl)silane was obtained 8.9 g (57%).

5. Diphenyldi(triphenylsilylpropyl)silane. From 5.6 g of lithium, 63 g (0.4 mole) of bromobenzene and 14 g (0.026 mole) of diphenyldi(trichlorosilylpropyl)silane was obtained 12.3 g (60%).

6. Phenylmethyldi(triphenylsilylpropyl)silane. From 7 g of lithium, 78.5 g (0.5 mole) of bromobenzene and 16 g (0.033 mole) of phenylmethyldi(trichlorosilylpropyl)silane was obtained 14.3 g (59.1%).

7. Phenylmethyldi(trimethylsilylpropyl)silane. From 7 g of lithium, 71 g (0.5 mole) of methyl iodide and 16 g (0.033 mole) of phenylmethyldi(trichlorosilylpropyl)silane was obtained 9.1 g (77.3%).

8. Dimethyldi(triethylsilylpropyl)silane. From 10 g of lithium, 78.5 g (0.72 mole) of ethyl bromide and 20 g (0.048 mole) of dimethyldi(trichlorosilylpropyl)silane was obtained 11.9 g (65.7%).

9. Dimethyldi(tripropylsilylpropyl)silane. From 10 g of lithium, 88.5 g (0.72 mole) of propyl bromide and 20 g (0.048 mole) of dimethyldi(trichlorosilylpropyl)silane was obtained 13.6 g (61.2%).

10. Dimethyldi(tributylsilylpropyl)silane. From 10 g of lithium, 98.5 g (0.72 mole) of butyl bromide and 20 g (0.048 mole) of dimethyldi(trichlorosilylpropyl)silane was obtained 15.3 g (58.1%).

11. Dimethyldi(triphenylsilylpropyl)silane. From 10 g of lithium, 113 g (0.72 mole) of bromobenzene and 20 g (0.048 mole) of dimethyldi(trichlorosilylpropyl)silane was obtained 10.5 g (32.7%).

12. Diphenyldi(trimethylsilylpropyl)silane. From 6.6 g of lithium, 67.4 g (0.475 mole) of methyl iodide and 17 g (0.032 mole) of diphenyldi(trichlorosilylpropyl)silane was obtained 7.1 g (54.6%).

SUMMARY

1. The addition of trichlorosilane to dialkyl(phenyl, chloro)diallylsilanes was studied in presence of benzoyl peroxide, platinized carbon and chloroplatinic acid.

2. It was shown that the activity of the double bond in diallyl derivatives of silicon increases with increasing size of alkyl radical (up to C_4) and when the latter are replaced by electronegative phenyl radicals or chlorine atoms.

3. Starting from products of addition of trichlorosilane to dialkyl(phenyl, chloro)diallylsilanes at the two double bonds, 12 previously undescribed silicohydrocarbons were synthesized. These contain three silicon atoms linked by propylene bridges.

4. Spectral investigations showed that the mode of addition of trichlorosilane to dialkyl(phenyl, chloro)diallylsilanes in presence of benzoyl peroxide, platinized carbon and chloroplatinic acid is contrary to the Markovnikov rule.

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DETERMINATION BY INFRARED SPECTROSCOPY OF THE STRUCTURE OF A SERIES OF SILICO-ORGANIC COMPOUNDS OBTAINED BY ADDITION OF TRICHLOROSILANE TO MONO- AND DIALLYL SILICON DERIVATIVES

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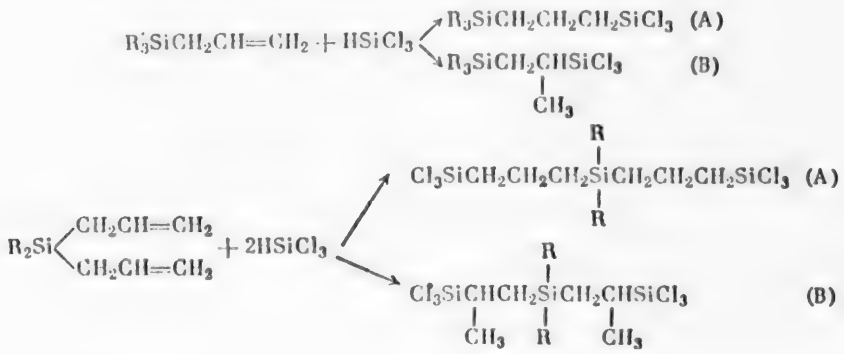
The object of the present investigation was the spectroscopic study of the structure of compounds obtained by addition of trichlorosilane to trichloroallyl- and dichlorodiallylsilane, and also of a series of silico-hydrocarbons synthesized from addition products of trichlorosilane to mono- and diallyl silicon derivatives (Table 1).

Addition of trichlorosilane to mono- and diallyl silicon derivatives was carried out in the presence of benzoyl peroxide, platinum on carbon, and of hydrochloroplatinic acid. This reaction can proceed both according to Markovnikov's rule (B), and contrary to Markovnikov's rule (A).



As seen from the structural formulas, the difference between (A) and (B) lies in the presence in (A) (besides radicals R) of CH_2 groups, and in (B), of an additional CH_3 group. Therefore, in the first part of the work we utilized the possibilities of the region of CH-valence vibrations (2800-3000 cm^{-1}) to determine the number of methyl and methylene groups [1].

Investigation of the Region of CH-Vibrations

In the region 2800-3000 cm^{-1} are found bands belonging to the valence vibrations of CH_2 and CH_3 groups. The strongest of these are the bands at 2930 and 2960 cm^{-1}, belonging to the unsymmetric vibrations in CH_2 and

TABLE 1

Prep. No.	Compound	Boiling point (pressure in mm)	Melting point	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated
1	$(CH_3)_3SiCH_2CH_2CH_2Si(CH_3)_3$	167—169°(748)	—	1.4218	0.7584	63.09	63.06
2	$(C_2H_5)_3SiCH_2CH_2CH_2Si(C_2H_5)_3$	140—141 (3)	—	1.4572	0.8253	89.98	90.12
3	$(C_3H_7)_3SiCH_2CH_2CH_2Si(C_3H_7)_3$	182—183 (4)	—	1.4590	0.8245	118.30	118.62
4	$(C_4H_9)_3SiCH_2CH_2CH_2Si(C_4H_9)_3$	216—218 (3.5)	—	1.4624	0.8304	146.06	145.92
5	$(C_6H_5)_3SiCH_2CH_2CH_2Si(C_6H_5)_3$	— —	120—121°	—	—	—	—
6	$(CH_3)_2SiCH_2CH_2CH_2Si(C_2H_5)_3$	116—118 (8)	—	1.4430	0.7980	76.58	76.92
7	$(CH_3)_3SiCH_2CH_2CH_2Si(C_2H_5)_3$	147—148 (8)	—	1.4461	0.8033	90.50	90.84
8	$(CH_3)_3SiCH_2CH_2CH_2Si(C_4H_9)_3$	170—172 (8)	—	1.4499	0.8102	104.35	104.39
9	$(CH_3)_2SiCH_2CH_2CH_2Si(C_6H_5)_3$	219—221 (4)	71—72	—	—	—	—
10	$Cl_3SiCH_2CH_2CH_2SiCl_3$	116,5—118 (5)	—	—	—	—	—
11	$(CH_3)_2Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	136—138 (6)		1.4448	0.8005	95.90	95.84
12	$(C_2H_5)_2Si[CH_2CH_2CH_2Si(C_2H_5)_3]_2$	224—226 (7)	—	1.4707	0.8500	131.75	131.92
13	$(C_3H_7)_2Si[CH_2CH_2CH_2Si(C_3H_7)_3]_2$	242—244 (6)	—	1.4687	0.8422	169.56	169.92
14	$(C_4H_9)_2Si[CH_2CH_2CH_2Si(C_4H_9)_3]_2$	273—275 (5)	—	1.4702	0.8450	206.31	206.32
15	$(C_6H_5)_2Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$	— —	114.5—116	—	—	—	—
16	$(CH_3)_2Si[CH_2CH_2CH_2Si(C_2H_5)_3]_2$	213—215 (7.5)	—	1.4678	0.8440	122.70	122.90
17	$(CH_3)_2Si[CH_2CH_2CH_2Si(C_4H_9)_3]_2$	236—238 (7)	—	1.4665	0.8400	150.78	151.40
18	$(CH_3)_2Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$	264—265 (8)	—	1.4680	0.8429	178.44	178.70
19	$(CH_3)_2Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$	— —	91—93	—	—	—	—
20	$C_6H_5(CH_3)Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	188—190 (5)	—	1.4840	0.8672	115.47	115.60
21	$C_6H_5(CH_3)Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$	— —	103—104	—	—	—	—
22	$(C_6H_5)_2Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	217—219 (5)	—	1.5218	0.9310	135.20	135.48
23	$Cl_2Si(CH_2CH_2CH_2SiCl_3)_2$	210—212 (2)	—	—	—	—	—

CH_3 groups respectively. An important property of these bands is their growth proportional to the number of homologous groups, thus affording the possibility of determining the number of them in the molecules [1]. In silicohydrocarbons this question was not investigated, but, taking into consideration the "barrier" properties of the silicon atom with regard to aliphatic groups [2], it could be assumed that the rule mentioned would be maintained. Besides this, the Si atom, and, especially, the groups $SiCl_3$ and $Si(C_6H_5)_3$ can exert an inductive influence on CH_2 and CH_3 groups, which must cause a certain amount of merging of bands and a change in their intensity in comparison with alkanes (compare the influence of aromatic rings [1]).

In studying the spectra of the compounds (Table 2) a good deal of attention was given to the band in the region 2952 cm^{-1}, corresponding, according to all indications, to the unsymmetrical (weakened) vibration of the CH_3 group.

Comparison of the intensities obtained for the peaks, both of the first three standard compounds and of the compounds investigated by us and shown in Table 2, shows high uniformity at the value ϵ_0. This demonstrates, on the one hand, the correctness of the number of CH_3 groups in all the compounds examined, and, on the other hand, rules out the possibility of formation of form (B), because in this case we would have a substantial overestimation in intensity of the peak at 2952 cm^{-1}. According to the data in the literature [1], the peak of the CH_3 group in a short aliphatic chain has an intensity of the order of 100 units for the group. Attention should also be drawn to the gradual increase of intensity of the band at 2915 cm^{-1} (CH_2 group) from zero in $(CH_3)_4Si$ to 65 units in hexamethyldisilylmethane, 85 units in hexamethyldisilylethane, and 125 units in hexamethyldisilylpropane. It is evident that on formation of form (B) the character of intensity growth would be different from this. In Table 3 intensities are shown of the peak of the CH_2 group in the silico-organic compounds investigated by us. On the left hand side of the table are shown several compounds obtained from monoallyl silicon derivatives, and on the right, from diallyl silicon derivatives.

As seen from the data in Table 3, the peak for CH_2 groups increases in intensity for compounds shown on the right side of the table twice as fast, i.e., in agreement with the form of structure (A). The $SiCl_3$ group lowers the intensity of the band for CH_2 groups, but this lowering, as is seen, is the same for hexachlorodisilylpropane and dichlorodi(trichlorosilylpropyl)silane (the compounds in the fourth line of the left- and right-hand parts of Table 3). The intensity of the bands 3050 and 3070 cm^{-1} belonging to C_6H_5 groups grows with the number of these radicals

TABLE 2

Intensity of the Peak at 2952 cm^{-1} (CH_3 groups)

Prep. No.	Compound	I_0	n	ϵ_0
1	$Si(CH_3)_4$	160	4	40
2	$(CH_3)_3SiCH_2Si(CH_3)_3$	275	6	46
3	$(CH_3)_3SiCH_2CH_2Si(CH_3)_3$	240	6	40
4	$(CH_3)_3SiCH_2CH_2CH_2Si(CH_3)_3$	250	6	42
5	$(CH_3)_3SiCH_2CH_2CH_2Si(C_6H_5)_3$	125	3	42
6	$(CH_3)_2Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	320	8	40
7	$(C_6H_5)_2Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	260	6	43

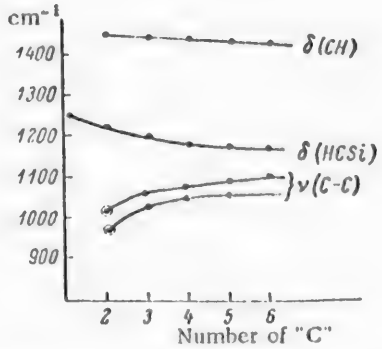
Note: I_0) intensity of band at a maximum; n) number of CH_3 groups in the silicon atom; E_0) intensity pertaining to one CH_3 group.

TABLE 3

Intensity of the Peak at 2912 cm^{-1} (CH_2 groups)

Prep. No.	Compound	I_0	Compound	I_0
1	$(CH_3)_3SiCH_2CH_2CH_2Si(CH_3)_3$	120	$(CH_3)_2Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	250
2	$(C_6H_5)_3SiCH_2CH_2CH_2Si(C_6H_5)_3$	90	$(C_6H_5)_2Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$	180
3	$(CH_3)_3SiCH_2CH_2CH_2Si(C_6H_5)_3$	130	$CH_3(C_6H_5)Si[CH_2CH_2CH_2Si(CH_3)_3]_2$	250
4	$Cl_3SiCH_2CH_2CH_2SiCl_3$	40	$Cl_2Si[CH_2CH_2CH_2SiCl_3]_2$	80

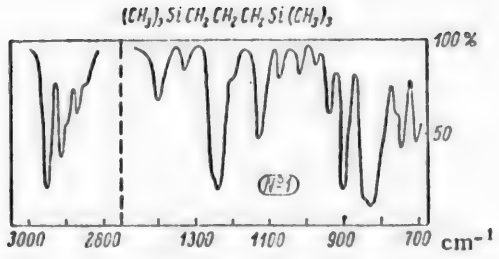
Note: I_0) intensity of band at a maximum.

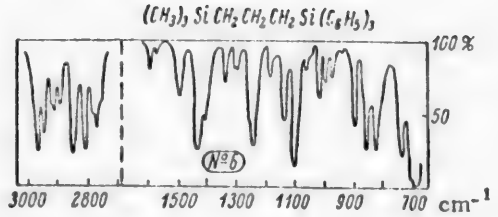


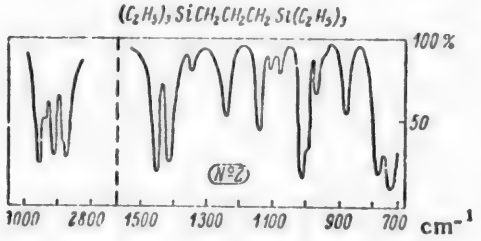
Magnitudes of characteristic frequencies of aliphatic radicals of normal structure attached to a silicon atom.

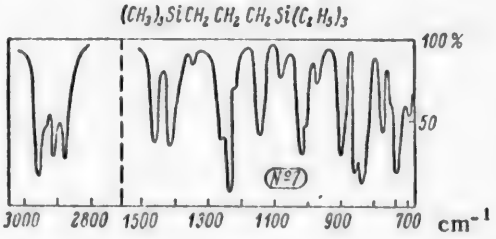
attached to the silicon atom. For example, the band at 3070 cm^{-1} has ϵ_0 120 units for triphenyltrimethyldisilylpropane (compound 9, Table 1) and 235 units for dimethyldi(triphenylsilylpropyl)silane (compound 19, Table 1).

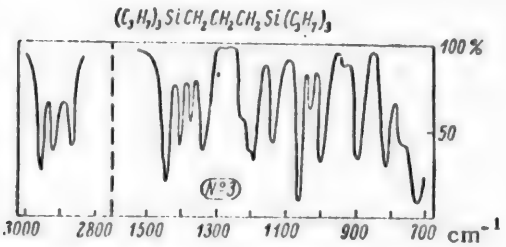
Proof of the structure of other compounds of this series, having attached to the silicon atom alkyl radicals with two or more carbon atoms, is difficult, because it is necessary to take into account the superimposition of bands belonging to CH_2 groups of the $Si(CH_2)_3Si$ complex and to the radicals themselves. Because of this, in this case it was more convenient to direct attention to the region 700-1700 cm^{-1}. According to the data given in work on this series [3], it is convenient to determine the type of radical attached to the silicon atom by means of the frequencies in the region 1150-1265 and 950-1100 cm^{-1} [2]. Investigation of this question leads to consequent dependence of the frequencies of the regions indicated on the length of the aliphatic chains (diagram). It is evident that the group $SiCH_2$-CH_2CH_2Si also has its own characteristic frequencies. Actually, a simple comparison of all spectra shown in the diagram permits the observation of two recurrent bands at approximately 900 and 1135-1140 cm^{-1}. Since these bands do not pertain to any aliphatic radicals, it is correct to confirm their belonging to the group $SiCH_2CH_2CH_2Si$. But since these bands are present in all spectra, both of the compounds containing only methyl and phenyl radicals and of compounds containing alkyl radicals with two or more carbon atoms, this same fact indicates a type (A) structure for

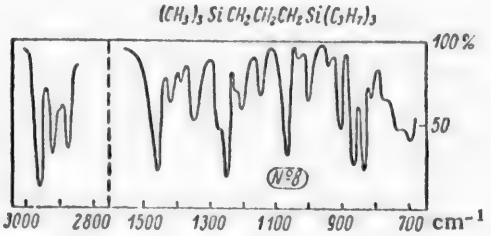

(CH3)3SiCH2CH2CH2Si(CH3)3
100%
50
№1
3000
2800
1300
1100
900
700
cm-1

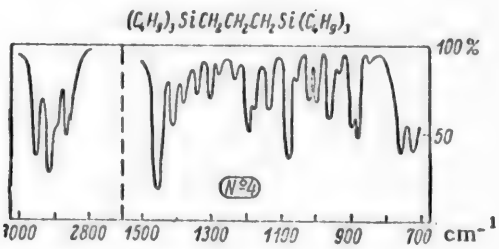

(CH3)3SiCH2CH2CH2Si(C6H5)3
100%
50
№6
3000
2800
1500
1300
1100
900
700
cm-1

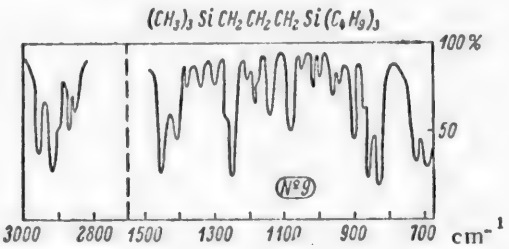

(C2H5)3SiCH2CH2CH2Si(C2H5)3
100%
50
№2
3000
2800
1500
1300
1100
900
700
cm-1

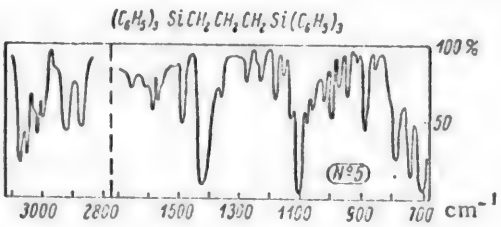

(CH3)3SiCH2CH2CH2Si(C2H5)3
100%
50
№7
3000
2800
1500
1300
1100
900
700
cm-1

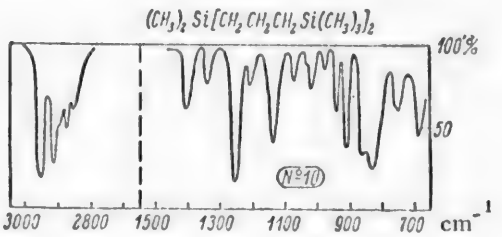

(C3H7)3SiCH2CH2CH2Si(C3H7)3
100%
50
№3
3000
2800
1500
1300
1100
900
700
cm-1

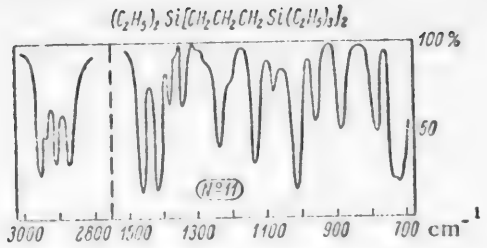

(CH3)3SiCH2CH2CH2Si(C3H7)3
100%
50
№8
3000
2800
1500
1300
1100
900
700
cm-1

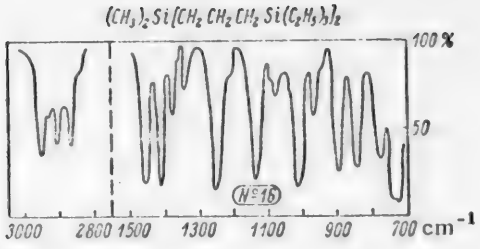

(C4H9)3SiCH2CH2CH2Si(C4H9)3
100%
50
№4
3000
2800
1500
1300
1100
900
700
cm-1

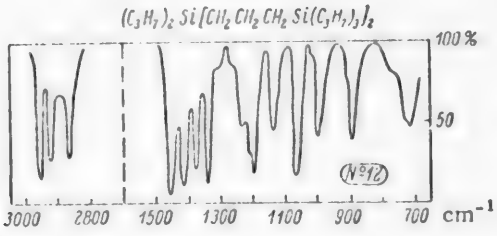

(CH3)3SiCH2CH2CH2Si(C4H9)3
100%
50
№9
3000
2800
1500
1300
1100
900
700
cm-1

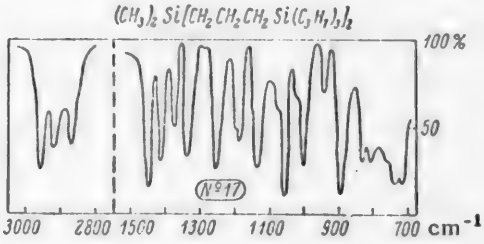

(C6H5)3SiCH2CH2CH2Si(C6H5)3
100%
50
№5
3000
2800
1500
1300
1100
900
700
cm-1

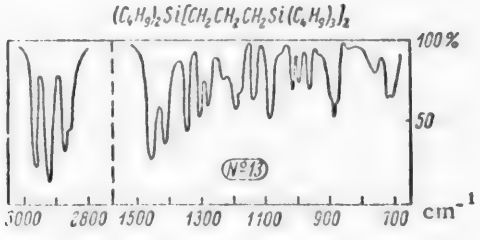

(CH3)2Si[CH2CH2CH2Si(CH3)3]2
100%
50
№10
3000
2800
1500
1300
1100
900
700
cm-1

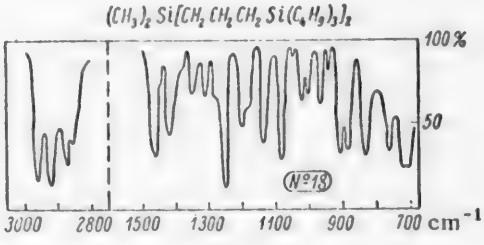

$(C_2H_5)_2Si[CH_2CH_2CH_2Si(C_2H_5)_3]_2$
100%
50
№11
3000 2800 1500 1300 1100 900 700 cm⁻¹

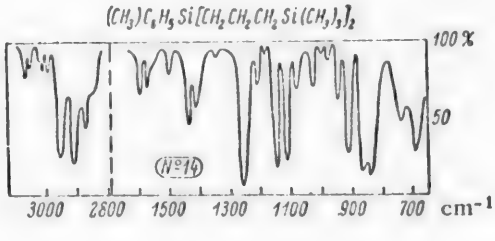

$(CH_3)_2Si[CH_2CH_2CH_2Si(C_2H_5)_3]_2$
100%
50
№16
3000 2800 1500 1300 1100 900 700 cm⁻¹

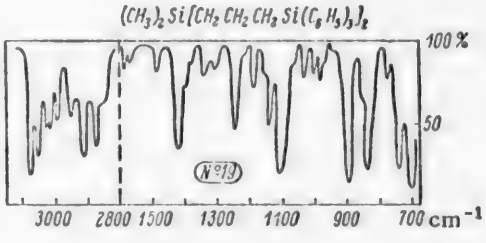

$(C_3H_7)_2Si[CH_2CH_2CH_2Si(C_3H_7)_3]_2$
100%
50
№12
3000 2800 1500 1300 1100 900 700 cm⁻¹

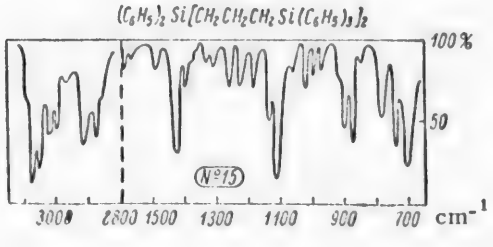

$(CH_3)_2Si[CH_2CH_2CH_2Si(C_3H_7)_3]_2$
100%
50
№17
3000 2800 1500 1300 1100 900 700 cm⁻¹

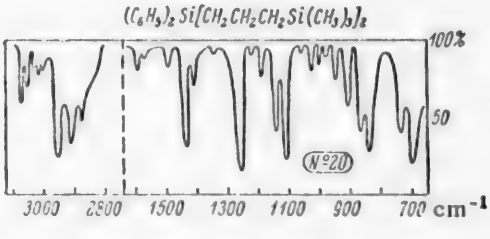

$(C_4H_9)_2Si[CH_2CH_2CH_2Si(C_4H_9)_3]_2$
100%
50
№13
3000 2800 1500 1300 1100 900 700 cm⁻¹


$(CH_3)_2Si[CH_2CH_2CH_2Si(C_4H_9)_3]_2$
100%
50
№18
3000 2800 1500 1300 1100 900 700 cm⁻¹


$(CH_3)C_6H_5Si[CH_2CH_2CH_2Si(CH_3)_3]_2$
100%
50
№14
3000 2800 1500 1300 1100 900 700 cm⁻¹


$(CH_3)_2Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$
100%
50
№19
3000 2800 1500 1300 1100 900 700 cm⁻¹


$(C_6H_5)_2Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$
100%
50
№15
3000 2800 1500 1300 1100 900 700 cm⁻¹


$(C_6H_5)_2Si[CH_2CH_2CH_2Si(CH_3)_3]_2$
100%
50
№20
3000 2800 1500 1300 1100 900 700 cm⁻¹

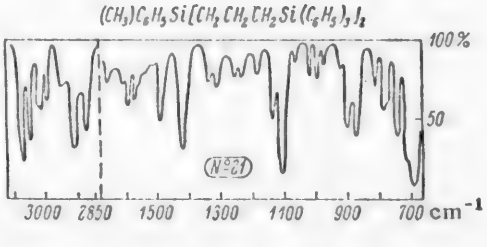

$(CH_3)C_6H_5Si[CH_2CH_2CH_2Si(C_6H_5)_3]_2$
100%
50
№21
3000 2850 1500 1300 1100 900 700 cm⁻¹

TABLE 4

Characteristic Frequencies of Radicals Attached to a Carbon Atom

Radical	Characteristic frequencies (in cm^{-1})	Numbers of spectra in which the given bands are found
CH_3	830, 865, 1250–1260	1, 6—10, 14, 16—20
C_2H_5	970, 1014, 1230	2, 7, 11, 16
$n\text{-}C_3H_7$	1030, 1065, 1205	3, 8, 12, 17
$n\text{-}C_4H_9$	1050, 1080, 1190	4, 9, 13, 18
C_6H_5	740, 1104, 1180, 1490, 1570, 1590, region above 3000 cm^{-1}	5, 6, 14, 15, 19, 20, 21

all the products investigated. In Table 4 are shown the most characteristic frequencies of radicals attached to a Si atom, as recorded in the data in the literature, and the numbers of the spectra, where they have been observed by us. Comparison of these data with the structure of the corresponding compounds shows complete agreement of spectral characteristics with structural formulas.

METHOD OF OBTAINING SPECTRA

Infrared spectra were obtained on an IKS-12 spectrometer in the region 700-1700 and 2800-3000 cm^{-1}. Prisms of NaCl and LiF were used. Spectra of liquid substances in the region 700-1700 cm^{-1} were investigated in the pure state in thin layers between plates of KCl; solid substances were mixed beforehand with potassium bromide (20 mg of the substance and 2 g of KBr) and compressed under a pressure of 12t /cm^2 into thin plates. In the region 2800-3100 cm^{-1} all substances were investigated as a 1% solution of CCl_4. The spectral curves obtained (recordings on tape) were subsequently converted into percentage transmittance.

SUMMARY

A study of the infrared spectra of products formed by addition of trichlorosilane to mono- and diallyl silicon derivatives in the presence of benzoyl peroxide, of platinum on carbon, and of hydrochloroplatinic acid showed that addition proceeds contrary to Markovnikov's rule, and that the compounds investigated have the following structure:

$$R_3SiCH_2CH_2CH_2SiR_3 \text{ и } R_3SiCH_2CH_2CH_2\underset{\displaystyle R}{\overset{\displaystyle R}{\underset{|}{\overset{|}{Si}}}}CH_2CH_2CH_2SiR_3.$$

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*Original Russian pagination. See C. B. Translation.

DIRECT BISAZO DYESTUFFS DERIVED FROM OXADIAZOLE AND THIODIAZOLE

II. COMPARATIVE INVESTIGATION OF THE ISOMERIC BISAZO DYESTUFFS DERIVED FROM THIODIAZOLE

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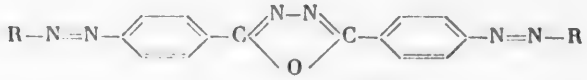
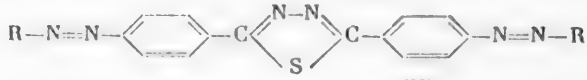
In a previous communication [1], we have described the bisazo dyestuffs containing in their molecules the oxadiazole (I) and thiodiazole (II) ring, and have called attention to the substantive properties of these dyestuffs in relation to cotton.



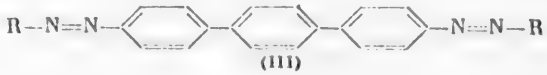
(I)



(II)

(R is the coupling component)

It still remains uncertain, however, to what extent the substantive properties of these dyestuffs is connected with the presence in their molecules of the heterocyclic rings, and to what extent it is to be attributed to the presence of the long chain of conjugated double bonds. It seemed to us that the answer to this question might be obtained best of all by comparing the affinity towards cotton of the dyestuffs I and II, with those of others which, though close to these in structure, did not contain the heterocyclic nucleus. Such dyestuffs are those derived from 4,4"-diamino-p-terphenyl (III), which have recently been studied by one of us [2].



(III)

Table 1 shows that, in spite of the presence in their molecules of chains of conjugated double bonds of the same length as are found in the dyestuffs derived from p-terphenyl, the dyestuffs I and II have no superiority in affinity towards cotton over III. On the contrary, the derivatives of thiodiazole to a lesser degree, and those of oxadiazole to a greater degree, are inferior in this respect to the last named.

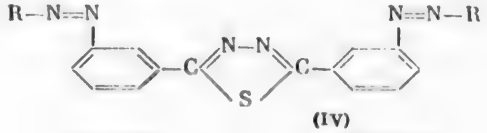
TABLE 1

Coupling component / Dyestuff	Affinity (in kcal/ mole)			
	Ash acid		Chicago SS acid	
	60°	80°	60°	80°
(I)	4.61	4.35	4.74	4.42
(II)	5.51	5.30	6.02	5.79
(III)	—	6.00	—	6.31

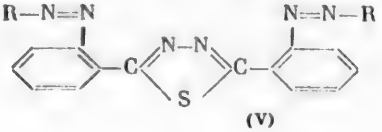
TABLE 2

Coupling component / Dyestuff	Affinity (in kcal/ mole)			
	Ash acid		Chicago SS acid	
	60°	80°	60°	80°
(II)	5.51	5.30	6.02	5.79
(IV)	3.23	2.63	3.42	3.00
(V)	1.83	1.67	1.47	0.91
(VI)	3.14	3.05	—	—

We also thought that it would be interesting for the estimation of the effect of the two factors mentioned above on the substantive character of dyestuffs of type II if we were to synthesize and study the dyestuffs IV and V, which are isomeric with them.



(IV)



(V)

In the former of this pair of dyestuffs, the azo groups are not connected together, nor with the central, heterocyclic, ring by means of a chain of conjugated double bonds, while such a chain is found in the latter of them, although the distance between the azo groups is appreciably shorter than in II.

Dyestuffs IV and V are not described in the literature. We obtained them according to the scheme used on an earlier occasion by one of us [1] for the synthesis of dyestuff II. The hydrazides of m- or o-nitrobenzoic acid were caused to react with phosphorus pentasulfide, as a result of which the thiodiazole ring was formed. Afterwards, the dinitro derivative of 2,5-diphenyl-1,3,4-thiodiazole was reduced by means of sodium disulfide into the corresponding diamine, which was then diazotized, and coupled in an alkaline medium with Ash* acid Chicago SS acid. Table 2 provides a comparison of the affinities towards cotton of dyestuffs IV and V, and their para-isomer II.

Table II shows that the interruption of the conjugation between the azo groups leads to an abrupt reduction in the affinity, giving then a value which is close to that affinity of the corresponding dyestuff prepared from 3,3'-diaminobiphenyl (VI), which differs from IV only in the absence of the thiodiazole ring.

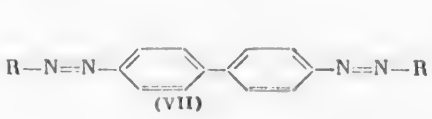
*Transliteration from the Russian original.

(VI)

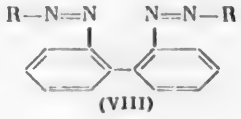
Thus, the effect of the heterogeneous ring in the absence of the chain of conjugated double bonds between the azo groups has, in the case under discussion, no effect on the dyeing properties of the dyestuff towards cotton.

It follows from the data presented in Table 2 that dyes V are even less substantive than their meta isomers (IV), although the molecules of V include the azo groups in the conjugated double bond chain. The shortening of the chain of conjugated double bonds between the azo groups, in comparison with dyestuff II, has in this case no appreciable effect, since chains of the same length are contained in the molecules of the substantive benzidine dyestuffs VII.

In all probability, we encounter here the same phenomenon as is observed in the investigation of dyestuffs derived from 2,2'-diaminobiphenyl (VIII), which has absolutely no affinity towards cotton.



(VII)



(VIII)

The cause of this phenomenon may be the nonlinear structure of the molecules of the dyestuff, or also the steric hindrance occurring in these molecules on account of the volume occupied by the substituents (the azo groups, and the radicals of the coupling components connected to them in the ortho-position in relationship to the inter-ring bond), and the impeding position of the benzene rings and thiodiazole ring, all located in a single plane. It is possible that both these factors, operating simultaneously, lead to practically complete loss of the substantive properties.

Table 3 provides a comparison of the colors of aqueous solution of dyestuffs II, IV and V. Dyestuffs IV and V, in which the azo groups are in the meta- or ortho-position to the thiodiazole ring, possess a higher color in solution in water than their para-isomers. The abrupt increase in the color in the case of the meta-isomers (IV) is associated with the interruption of the chain of conjugated bonds between the two chromophoric systems in the molecules of the dyestuffs. As to dyestuff V, the increase in color must be attributed both to the shortening of the chain of conjugated double bonds between the azo groups as compared with that present in the para-isomers, and to the steric hindrance which has already been discussed above. It is questionable, however, whether such a shortening of the chain would lead to so considerable an increase in the color, since the corresponding benzidine dyestuffs (VII), which have a chain of conjugated double bonds of the same length, have an absorption maximum displaced by 50-60 mμ towards the longer wave-length region of the spectrum, as compared with dyestuffs of type V. This makes it possible with considerable confidence to draw the conclusion that the steric hindrance in the molecules of dyestuffs of type V is of great importance.

TABLE 3

Coupling component / Dyestuff	λ_{max} mμ	
	Ash acid	Chicago SS acid
(II)	553	588
(IV)	520	528
(V)	536	536

EXPERIMENTAL

2,5-Bis-(3-Nitrophenyl)-1,3,4-Thiodiazole. 3 grams of N,N'-bis-(3-nitrobenzoyl)-hydrazine were dissolved with heating under a reflux condenser in 20 ml of dry nitrobenzene, and to the boiling liquid were added 6 grams of phosphorus pentasulfide, prepared according to the method described in [3]. Effervescence and darkening of the liquid took place during this process. The mixture was then boiled for a further 15 minutes. On the following day the residue which had separated out on cooling was filtered off, washed with benzene to remove residual nitrobenzene, dried, washed with a warm 3% solution of sodium hydroxide and then with water, dried again, and submitted to repeated treatment with carbon disulfide. It was then recrystallized from glacial acetic acid. Yield: 1.2 g (40% of theoretical).

Analysis: N = 16.79%; 16.94%. Calculated N for $C_{14}H_8O_4N_4S$ = 17.07%.

The product obtained was a pale-yellow powder with a melting point of 240-241°. It was insoluble in water and carbon disulfide, but soluble in pyridine, and, on heating, in glacial acetic acid.

2,5-Bis-(2-nitrophenyl)-1,3,4-thiodiazole was obtained in a similar way from N,N'-bis-(2-nitrobenzoyl)-hydrazine. Yield 1.15g (39%).

Found %: N 16.63, 16.61. Calculated for $C_{14}H_8O_4N_4S$, %: 17.07.

The product was a pale-yellow powder, m.p. 208°, insoluble in water and carbon disulfide, soluble in pyridine, and on heating in glacial acetic acid and toluene.

2-5-Bis-(3-aminophenyl)-1,3,4-thiodiazole was obtained from 2,5-bis-(3-nitrophenyl)-1,3,4-thiodiazole, the reduction being carried out under the same conditions as those previously used for the preparation of 2,5-bis-(4-aminophenyl)-1,3,4-thiodiazole [1]. 2.5 g of the nitrocompound were heated under reflux to dissolve in 20 ml of pyridine, and then during one hour there was added to the boiling solution 140 ml of a sodium disulfide solution prepared by dissolving 32 g sulfur and 240 g crystalline sodium sulfide ($Na_2S \cdot 9H_2O$) in a mixture of 625 ml water and 100 ml pyridine. In the course of this process the color changed from yellow to dark green. The solution was boiled for a further hour and then cooled, and the contents of the flask poured into one liter of water. On the following day the precipitate formed was filtered off, washed several times with water, dried, and recrystallized twice from isoamyl alcohol. Yield 1.9g (93%).

Analysis: NH_2• = 11.81%; 11.81%. Calculated NH_2 for $C_{14}H_8N_2S(NH_2)_2$ = 11.94%.

The product obtained was a pale-yellow powder with melting point 239° (according to [5] it is 239-240°). It is easily soluble in pyridine and isoamyl alcohol, but insoluble in water.

2,5-Bis-(2-Aminophenyl)-1,3,4-Thiodiazole was obtained by the reduction of 2,5-bis-(2-nitrophenyl)-1,3,4-thiodiazole. The reduction was carried out in the same way as for the previous product; the amine was purified by recrystallization from alcohol. From 0.9 gram of the nitro-compound, 0.67 gram of the amine was obtained (91% of theoretical).

Analysis: NH_2 = 11.90%; 11.93%. Calculated HN_2 for $C_{14}H_8N_2S(NH_2)_2$ = 11.94%.

The product obtained was a yellow powder, with melting point 216-217°. It is insoluble in water, but soluble in glacial acetic acid, and on heating in alcohol and in benzene.

To demonstrate that the amine prepared is a derivative of 2,5-diphenyl-1,3,4-thiodiazole, we subjected it to a deamination process. 0.2 gram of the diamine was dissolved in a mixture of 25 ml water and 2 ml concentrated hydrochloric acid, and after the solution had been cooled to 0°, 0.11 gram of sodium nitrite was added. The solution of the diazo compound obtained in this way was filtered, and with thorough stirring 2 grams of potassium hypophosphite (KH_2PO_2) was added. On the following day the product of deamination which had settled out was filtered off and recrystallized from alcohol. Its melting point was 145-146° (compared with the figure of 141-142° contained in the literature [6]).

3,3'-Diaminobiphenyl was obtained by the reduction of 3,3'-dinitrobiphenyl. The latter was synthesized according to a scheme already published [7] by the nitration of the diacetyl derivative of benzidine, saponifica-

• The analysis was carried out by means of potentiometric titration by means of a 0.01 N solution of sodium nitrite [4].

tion of the product obtained in this way, and subsequent deamination of the 3,3'-dinitrobenzidine. In distinction from the procedure followed in [7], we carried out the deamination by means of potassium hypophosphite. Into a mixture consisting of 4.5 grams of sodium nitrate and 45 ml of concentrated sulfuric acid and held at 10°, 8 grams of the 3,3'-dinitrobenzidine was introduced, and the mass stirred for an hour. Subsequently 45 ml of glacial acetic acid was added, and the mixture stirred for a further 15 minutes; poured on to ice. There were then added, with mixing, 80 grams of potassium hypophosphite. There was immediately formed a dark-yellow precipitate, which, after 24 hours, was filtered off, washed with water, and dried. M.p. = 194-195° (compared with the figure of 196-198° contained in the literature [7]; after distillation of impurities away at a temperature above 200° at a pressure of 10^{-3} mm Hg, the melting point was 200°).

The reduction of 3,3'-dinitrobiphenyl was carried out by means of hydrazine hydrate in alcoholic solution, according to a method published earlier [8]. 3.5 grams of 3,3'-dinitrobiphenyl were stirred into 35 ml of alcohol with heating under reflux on a water bath. 6 ml of hydrazine hydrate was added, and then in small portions nickel was introduced. The reduction was regarded as completed when the evolution of nitrogen ceased. The solution was filtered away from the nickel, and the filtrate evaporated. The amine then separated out in the form of an oil which solidified on cooling. The purification of the amine obtained was performed in the following way: it was dissolved in anhydrous benzene and hydrogen chloride gas was passed into the solution. The amine hydrochloride which separated during this treatment did not melt up to 350°. Yield 2.3 g (63% of theoretical).

Analysis: NH_2 = 12.25%; 12.25%. Calculated NH_2 for $C_{12}H_{10}Cl_2(NH_2)_2$ = 12.45%.

The amine was separated from the hydrochloride by the addition of alkali to the aqueous solution of the salt. It was a talc-colored powder with melting point 93° (compared with 92-94° in the published literature [7]).

Dyestuffs Derived from 2,5-Bis-(3-Aminophenyl)- and 2,5-Bis-(2-Aminophenyl)- Derivatives of 1,3,4-Thiodiazole. The diazotization of all the amines was carried out by the addition of the calculated quantity of sodium nitrite to the solution of the amines in hydrochloric acid. 2,5-Bis-(2-aminophenyl)-1,3,4-thiodiazole was diazotized at 30°, and the two other amines at 0-5°. The coupling with A_{III} acid and Chicago SS acid was performed in an alkaline medium, to which the necessary quantity of soda was added. When the dyestuffs were separated from the aqueous solutions some difficulty was experienced, since the dyestuffs obtained from 2,5-bis-(2-aminophenyl-1,3,4-thiodiazole were too soluble in water for the addition of common salt to cause them to precipitate. We effected the separation from solution by the addition of hydrochloric acid: the precipitate obtained was filtered off and dissolved in the minimum quantity of water. To the aqueous solution was then added under gentle heating the quantity of soda needed to convert the dyestuff into the sodium salt. The solution obtained was purified by means of a chromatographic method on aluminum oxide, and then evaporated to dryness on a water bath.

The dyestuffs obtained from 2,5-bis-(3-aminophenyl)-1,3,4-thiodiazole and 3,3'-diaminobiphenyl were purified from mineral impurities by the acetate method [9], and then their aqueous solutions were submitted to chromatography on aluminum oxide. All the dyestuffs were analyzed by the method described in [10].

The affinity of the dyestuffs for cotton was determined according to the method described in [11], the size of the affinity being calculated on the basis of results obtained on dyeing with a vat modulus of 1:100, dyestuff concentration of 0.0001 molar, and sodium chloride concentration 0.02 molar with respect to the dyestuff solution. The dyeing was carried out at 60 and 80° up to an equilibrium condition. Then concentrations of the dyestuffs in the solutions were determined by a colorimetric method, using the photoelectric colorimeter FÉK-M. Control solutions for the period of all the dyeing processes were heated in a thermostat at the same time as the dyestuff solutions.

The maximum absorption of the dyestuff solutions was determined on the spectrometer SF-2M.

SUMMARY

1. There have been synthesized disazo dyestuffs from 2,5-bis-(3-aminophenyl)- and 2,5-bis-(2-aminophenyl)-derivatives of 1,3,4-thiodiazole. The affinity of these towards cotton has been examined, together with their color in aqueous solution.

2. Interruption of the conjugation between the two chromophoric groups of the systems found in the dyestuff molecules derived from 2,5-bis-(3-aminophenyl)-1,3,4-thiodiazole leads to a sudden increase in the color and a diminution in the substantive character, in comparison with the isomeric dyestuffs derived from 2,5-bis-(4-aminophenyl)-1,3,4-thiodiazole, in which the azo groups are situated in para-position with respect to the inter-ring bond.

3. The low affinity towards cotton, and the high color of the dyestuffs derived from 2,5-bis-(2-aminophenyl)-1,3,4-thiodiazole, in which the azo groups occur in the ortho-positions with respect to the inter-ring bond, permits us to assumption that considerable steric hindrance is present in these molecules.

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THE REACTIONS OF ISOPRENE OXIDE WITH HYDROGEN SULFIDE, MERCAPTANS AND KETONES

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The chemical properties of isoprene oxide, in distinction from those of divinyl oxide, have up to now been studied to a very limited extent. When isoprene oxide is submitted to the action of hydrobromic acid, isomerization takes place with the production of tiglaldehyde [1]. The direction in which the addition of alcohols to isoprene oxide proceeds is determined to a considerable extent by the nature of the catalysts used in such reactions [2]. Ammonia and amines combine with isoprene oxide in accordance with the Markovnikov Rule [3], in the main, though not exclusively.

In the development and extension of these investigations, we have carried out a study of the reactions of isoprene oxide with hydrogen sulfide, and with certain mercaptans. The addition of hydrogen sulfide to isoprene oxide was carried out in aqueous alcohol solution, in the presence of hydrated barium oxide and at room temperature. One product, 2-methylbutene-3-thiol-1-ol-2 (I) has been isolated. The presence in this compound of a primary mercapto group has been confirmed by the Rheinboldt test [4]. Consequently, the combination of hydrogen sulfide with methylvinylethylene oxide takes place in accordance with the Markovnikov Rule.

$$HS-CH_2-\underset{\displaystyle CH_3}{\overset{|}{C}}OH-CH=CH_2 \quad (I)$$

The results obtained are in harmony with the data on the combination of hydrogen sulfide with other unsymmetrical doubly substituted oxides of ethylene, such as the oxides of methylethylethylene and methylphenylethylene [5]. The addition of ethylmercaptan and propylmercaptan to isoprene oxide was carried out in the presence of an alkaline catalyst – sodium mercaptide and boron fluoride. In both cases it has been established that a mixture of the two isomeric thioethers is formed. When the combination of isoprene oxide with ethyl- and propylmercaptans is carried out in the presence of sodium mercaptide, the reaction takes place primarily in accordance with the Markovnikov Rule, but not exclusively so: a mixture of the thioethers II and III is formed, the primary thioether II predominating.

$$CH_2=CH-\underset{\displaystyle OH}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-CH_2SR \quad (II) \qquad CH_2=CH-\underset{\displaystyle SR}{\overset{\displaystyle CH_3}{\overset{|}{\underset{|}{C}}}}-CH_2OH \quad (III)$$

R=CH_3, C_2H_5.

TABLE 1

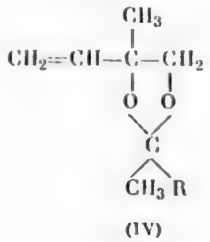
Products of the Combination of Hydrogen Sulfide and Mercaptans with Isoprene Oxide

Substance	Boiling point (pressure = 11 mm)	n_D^{20}	d_4^{20}	MR_D		% S		% OH		Yield (wt.%)
				found	calculated	found	calculated	found	calculated	
(I)	140–141.5°	1.5135	1.0581	33.54	34.16	26.89	27.13	14.03	14.39	25
(II) R = C_2H_5	81–82.5	1.4875	0.9708	43.29	43.58	21.90	21.92	12.58	11.63	26.8
(III) R = C_2H_5	106–107.5	1.5032	0.9905	43.58	43.58	21.79	21.92	12.45	11.63	15.3
(II) R = C_3H_7	97–98.5	1.4890	0.9581	48.19	48.20	20.10	20.00	10.48	10.61	26.2
(III) R = C_3H_7	121.5–123	1.5039	0.9832	48.18	48.20	19.81	20.00	10.48	10.63	15.6

In the presence of boron fluoride, the same mixture of thioethers is produced, but now the predominant compound is that with the tertiary thioether group (III). This change is due to the change in the polarization of isoprene oxide during the reaction under the influence of the boron trifluoride. The evidence that the formulas of the compounds produced correspond to II and III was found in a study of the rate of their benzoylation: the hydroxyl group in substance II undergoes benzoylation at only one sixth of the rate of that in substance III. Comparison of the constants also shows that substance III contains a primary alcoholic hydroxyl, while substance II contains a secondary alcoholic hydroxyl. The characteristics of the products obtained are given in Table 1.

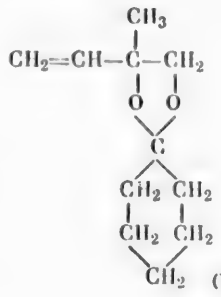
The results show that the combination of mercaptans with isoprene oxide in the presence of a basic catalyst takes place in a manner analogous to that of alcohols [2]. In the presence of boron trifluoride alcohols combine with isoprene oxide exclusively with the formation of ternary ethers: that is, violation of Markovnikov's Rule occurs; under the conditions, the mercaptans also form a mixture in which the tertiary thioethers are the predominant products.

In conclusion, we have also investigated the formation of dioxalanes, with a yield of from 40% to 50% by the reaction of acetone with isoprene oxide (IV, when R = CH_3); or of methylethylketone with the oxide (IV, R = C_2H_5); or the cyclohexanone with it (V). There has lately been a considerable growth of interest in dioxalanes on account of the possibility of using them as plasticizers, solvents, and pharmaceutical materials. The reactions were carried out in the presence of the etherate of boron trifluoride.



(IV)

R=CH_3, C_2H_5.



(V)

The characteristics of the products obtained are given in Table 2.

EXPERIMENTAL

Isoprene oxide was obtained by means of the oxidation of isoprene by acetyl hydroperoxide in ethereal solution [6].

The combination of hydrogen sulfide with isoprene oxide. 10 grams of hydrated barium oxide were thoroughly suspended in 75 ml of 75% alcohol, and the reaction mixture was saturated with hydrogen sulfide. Then, during a period of two hours, 20 g of isoprene oxide was added in drops during continued bubbling in of the hydrogen sulfide.

TABLE 2

Products of the Combination of Ketones with Isoprene Oxide (dioxalanes)

Substance	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	% C found	% C calculated	% H found	% H calculated	Yield (wt.%)
(IV) R = CH_3	130–132° (760)	1.4208	0.9114	39.49	39.69	67.43	67.57	9.75	9.92	38.8
(IV) R = C_2H_5	152–154 (760)	1.4321	0.9156	44.20	44.31	69.45	69.19	10.15	10.09	35.0
(V)	81–82.5 (11)	1.4622	0.9799	51.08	51.19	72.21	72.49	9.79	9.95	48.6

After the addition of the calculated quantity of sulfuric acid to bring about the precipitation of the barium ions, the reaction mixture was extracted with ether, the ethereal extract being dried by means of sodium sulfate. Fractional distillation produced 7 g of 2-methylbutene-3-ol-2-thiol-1 (I). The appearance of a red coloration on the addition of sodium nitrite (Rheinboldt test) shows that the product obtained contains a primary, and not a tertiary, mercapto group.

The combination of ethylmercaptan and propylmercaptan with isoprene oxide. 1) In the presence of sodium mercaptide. To 22.1 g of freshly redistilled ethylmercaptan were added 0.3 g sodium and 30 g isoprene oxide. The reaction was carried out in a sealed tube at 100 to 110° during a period of 14 hours. Distillation yielded 14 g of 2-methyl-1-thioethoxy-3-ol-2, and 8 g of 2-methyl-2-thioethoxybutene-3-ol-1. In an experiment carried out in a similar way using 27.1 g propylmercaptan and 30 g isopropyl oxide, 15 g of 2-methyl-1-thiopropoxybutene-3-ol-1 and 9 g 2-methyl-2-thiopropoxybutene-3-ol-1.

2) In the presence of the etherate of boron trifluoride. To a solution of 22.1 g of ethylmercaptan and 0.15 ml of the etherate of boron trifluoride in 100 ml of dry ether there is added gradually, during cooling with ice-cold water and with shaking 30 g isoprene oxide. The reaction mixture is heated for 12 hours at 60°. There is produced 3 g of 2-methyl-1-thioethoxybutene-3-ol-2, and 10 g of 2-methyl-2-thioethoxybutene-3-ol-1. In a similar experiment using 44 g isoprene oxide, 40 g propylmercaptan and 0.3 ml of the etherate of boron trifluoride in dioxan solution (heated for 14 hours at 90°) there was obtained 6 g of 2-methyl-1-thiopropoxybutene-3-ol-2, and 24 g 2-methyl-2-thiopropoxy-3-butenol-1.

The interaction of isoprene oxide with ketones. To 1 mole of the ketone, cooled to -10°, containing 0.4 to 0.5 g of the etherate of boron trifluoride, there was added gradually 0.2 mole of the ketone.* The reaction mixture was allowed to stand for 2 hours during the cooling, and then for 14 hours at room temperature, after which it was washed with a saturated potash solution. The upper layer was dried with potash and distilled. The characteristics of the product obtained are shown in Table 2.

SUMMARY

1. The combination of hydrogen sulfide with isoprene oxide takes place in accordance with the Markovnikov Rule. When combination takes place between ethyl- and propyl-mercaptan and isoprene oxide in the presence of sodium mercaptide, the yield of primary thioethers is about 1.5 times as great as that of the tertiary, while in the presence of the etherate of boron trifluoride the yield of the tertiary thioethers is about 3 times that of the primary.

2. From isoprene oxide and ketones in the presence of the etherate of boron trifluoride, the corresponding cyclic acetals – the dioxalanes – are obtained with a yield of 40-50%.

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*As in the Russian. But the 0.2 mole presumably refers to the isoprene oxide, and the 1 mole to the ketone – Translator's note.

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* Original Russian pagination. See C. B. Translation.

THE CLAISEN REARRANGEMENT OF THE ALLYL ESTERS OF THIOPHOSPHORIC ACID

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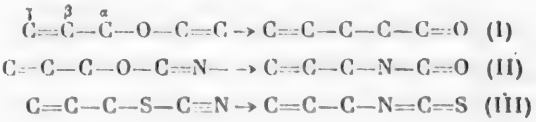
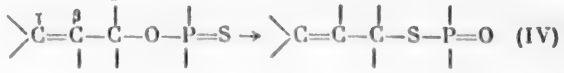
The nature of the Claisen rearrangement is known to consist in the isomerization of allyl ethers of enols and phenols into C-allyl derivatives (I) [1]. A similar rearrangement takes place when substituted derivatives of iminoallyl ethers (II) are heated [2], or when allyl esters of thiocyanic acid (III) are heated [3].

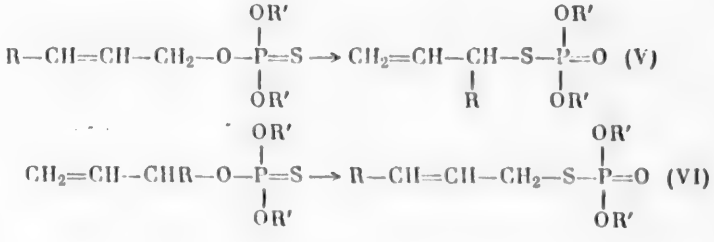


If the oxygen atom in (I) is replaced by nitrogen, the rearrangement does not take place. If substituents are present in the allyl group (alkyl or phenyl groups being used) in the α- or γ-carbon atom positions, the rearrangement often takes place together with inversion [4].

It seemed to us a matter of interest to attempt to elucidate the possibility of the occurrence of the Claisen rearrangement with esters of thiophosphoric acid, in which one of the ester radicals was an unsaturated radical. The allyl esters of thiophosphoric acid contain an atomic grouping analogous to that of compound I, in which the double C = C bond is replaced by the linkage P = S (IV).



It might be expected that, when substituents are present in the α- or γ-position in the allyl group, the rearrangement would be accompanied by inversion.



The isomerization of the esters of thiophosphoric acid was discovered in 1912 [5]. When the O,O,O-esters of thiophosphoric acid are heated with alkyl halides, rearrangement takes place to given O,O,S-esters of thiophosphoric acid.

$$(RO)_3P{=}S + R'Hal \rightarrow (RO)_2P(=O){-}SR' + RHal$$

It was subsequently found that similar isomerization may take place in certain cases even in the absence of the alkyl halide. Thus systox (diethyl-β-mercaptoethylthiophosphate), and compounds of a similar kind, isomerize on heating into thiol derivatives [6]. There exist data on the thermal isomerization of dialkyl-p-nitrophenyl esters of thiophosphoric acid, and a number of other compounds [7].

Dimethyl, diethyl and di-n-butyl esters of thiophosphoric acid have been obtained in the course of this work by the method of Pishchimuka, by the action of the acid chlorides of the corresponding dialkylthiophosphoric acids on the alcoholate of allyl alcohol. The reaction was performed with heating in benzene solution. The yields of the thioesters were usually around 40-45%. (See numbers 1, 3 and 5 in the Table).

$$(RO)_2P(=S)Cl + NaO{-}CH_2{-}CH{=}CH_2 \rightarrow (RO)_2P(=S){-}O{-}CH_2{-}CH{=}CH_2 + NaCl$$

The double bond in these compounds was determined quantitatively: ozonolysis permitted of the identification of formaldehyde in the form of its condensation product with dimedon. The infra-red spectrum of dimethylallyl thiophosphate has been obtained. The absence of an intensive absorption band in the region of 1300-1260 cm^{-1}, which is characteristic of the P = O bond, points to the absence of the thionyl grouping in the molecule [8].

The dialkylallyl esters of thiophosphoric acid so obtained were submitted to thermal isomerization. By analogy with the thermal isomerization of thiocyanic acid (III), it could be expected that the unsaturated esters of thiophosphoric acid would undergo isomerization easily in comparison with esters containing alkyl radicals. The experiments have confirmed this conclusion. The O,O,S-dialkylallylphosphates obtained by the isomerization have higher boiling points, specific gravity and refractive index (see numbers 2, 4 and 6 in the Table) than the esters which form their starting point.

$$(RO)_2P(=S){-}OCH_2{-}CH{=}CH_2 \rightarrow (RO)_2P(=O){-}S{-}CH_2{-}CH{=}CH_2$$

When the acid chlorides of dimethyl- and diethylallylphosphoric acid were caused to react with the alcoholate of crotyl alcohol, the corresponding dimethylcrotyl and diethylcrotyl esters of thiophosphoric acid (numbers 7 and 9 in the Table) were obtained. The ozonolysis of substance 9 produced acetaldehyde. The thermal isomerization of substances 7 and 9 produced products (numbers 8 and 10 respectively) with higher boiling point (a difference of 12-13° was found), specific gravity and refractive index. The ozonolysis of substances 8 and 10 produced formaldehyde in both cases, this being identified in the form of its condensation product with dimedon. The conclusion to be drawn from these results is that the thermal isomerization of dialkylcrotyl esters is accompanied by inversion (as in equation V).

Somewhat different results were obtained by the interaction of the alcoholate of methylvinylcarbinol on the acid chlorides of dimethyl- and diethylthiophosphoric acids. Two products were isolated from each of these reactions. Low-boiling products, obtained in small quantity, contained a considerably lower percentage of phosphorus than that calculated for O,O-dialkyl-O-α-methylallylthiophosphate; they had a high specific gravity; bromination, performed in chloroform solution, revealed the absence of a double bond in these compounds. In the infra-red spectrum of the low-boiling product obtained from the interaction of the acid chloride of diethylthiophosphoric acid with the alcoholate of methylvinylcarbinol, frequencies characteristic of the double bond were absent, while the presence of an intense absorption band with a maximum at 1263 cm^{-1} points to the presence of a thiol structure.

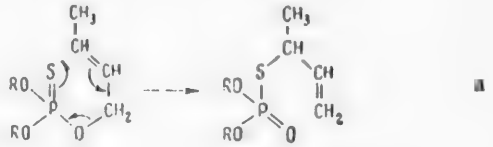
On the basis of these data, we have come to the conclusion that the products obtained are O,O-dimethyl-S-methyl-, and O,O-diethyl-S-ethylthiophosphates. The constants of these products are close to the values given for the compounds named in the literature.

The high-boiling products obtained in the reaction under consideration for substances 11 and 12, boiled some 25-30° higher than the corresponding O,O-dialkyl-O-crotylthiophosphates. When they are heated for 4 hours at 140°, they remain unchanged. It is evident that the isomerization of the O,O-dialkyl-O-α-methylallylthiophosphates takes place in the carrying out of the reaction itself. In the infra-red spectra of substance 12, there is an intense absorption band with a maximum at 1263 cm^{-1}, which is a further confirmation of the presence of the thiol structure.

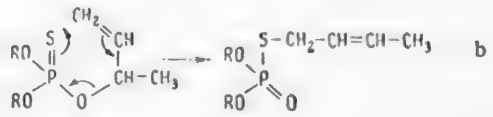
Ozonolysis of the high-boiling product obtained by the reaction of dimethylthiophosphoric acid chloride on the alcoholate of methylvinylcarbinol yielded acetaldehyde. It follows that the thermal isomerization of O,O-dialkyl-O-α-methylallyl esters of thiophosphoric acid also takes place with inversion, and that as a result of this there are obtained O,O-dialkyl-S-crotyl esters of thiophosphoric acid (according to equation VI). So as to make this opinion more conclusive, the O,O-diethyl-S-crotyl ester of thiophosphoric acid was synthesized by the method given in [9], by acting on the sodium salt of the diethyl ester of thiophosphoric acid with crotyl chloride.

$$(C_2H_5O)_2\overset{\overset{S}{\|}}{P}ONa + ClCH_2{-}CH{=}CH{-}CH_3 \rightarrow (C_2H_5O)_2\overset{\overset{O}{\|}}{P}{-}S{-}CH_2CH{=}CH{-}CH_3$$

It was shown that the alkylation of the salts of dialkylthiophosphoric acid takes place with transfer of the reaction center. We have shown earlier that the action of primary chlorides of the allyl type with the salts of dialkylphosphoric acids takes place without allyl rearrangement [10]. The constants of the product obtained by this reaction (no. 12 in the Table), and by means of an alternative synthesis, are completely in agreement. The formation of small quantities of O,O-dialkyl-S-alkylthiophosphates during the reactions of the acid chlorides of dialkylthiophosphoric acids with the alcoholate of methylvinylcarbinol may be explained by the partial disproportionation of the O,O-dialkyl-S-crotyl esters of thiophosphoric acid during the reaction.

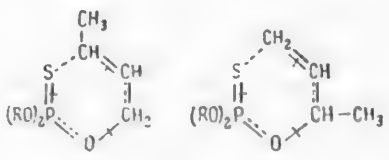


a



b

It follows from the work reported here that the dialkylallyl esters of thiophosphoric acid, in which methyl-substituents are present in the allyl group in the α- or γ-position, undergo rearrangement with inversion on heating. The results obtained, from our point of view, may best be explained if it is supposed that the thermal isomerization of the unsaturated esters of thiophosphoric acid takes place through a cyclic mechanism in one act, according to the scheme (a, b) above.



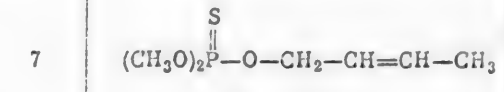
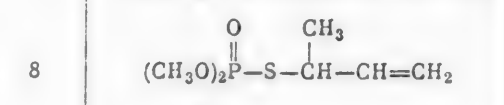
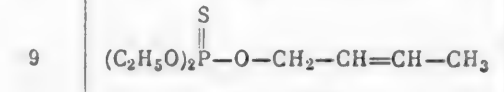
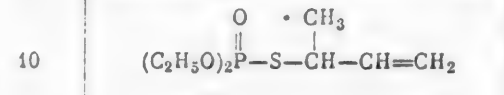
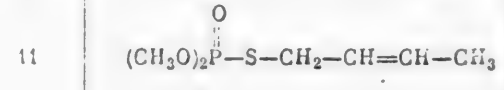
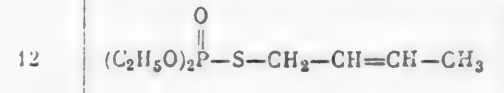
It may be supposed, in harmony with the ideas of Ya. K. Syrkin [11], that the process of thermal isomerization takes place through intermediate active six-membered complexes with reduced activation energy, the decomposition of which leads to the same products.

TABLE

Unsaturated O,O-Dialkyl-O-Allyl, and O,O-Dialkyl-S-Allylthiophosphates

Number of product	Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		% P		Yield (in %)
					found	calculated	found	calculated	
1	$(CH_3O)_2\overset{S}{\overset{\|}{P}}-O-CH_2-CH=CH_2$	88° (10)	1.4683	1.1451	44.20	44.31	17.33	17.03	44.3
2	$(CH_3O)_2\overset{O}{\overset{\|}{P}}-S-CH_2-CH=CH_2$	90—91 (2.5)	1.4798	1.1848	43.62	44.02	17.45	17.03	27
3	$(C_2H_5O)_2\overset{S}{\overset{\|}{P}}-O-CH_2-CH=CH_2$	82 (4 мм)	1.4605	1.0773	53.42	53.55	14.70	14.76	43
4	$(C_2H_5O)_2\overset{O}{\overset{\|}{P}}-S-CH_2-CH=CH_2$	107—108 (5)	1.4710	1.1067	53.04	53.26	15.06	14.76	30.1
5	$(C_4H_9O)_2\overset{S}{\overset{\|}{P}}-O-CH_2-CH=CH_2$	106—107 (1)	1.4635	1.0208	71.93	72.02	11.79	11.65	13
6	$(C_4H_9O)_2\overset{O}{\overset{\|}{P}}-S-CH_2-CH=CH_2$	138—140 (2)	1.4673	1.0349	71.44	71.72	—	—	20

TABLE (Continuation)

Number of product	Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		% P		Yield (in %)
					found	calculated	found	calculated	
7		82—83° (3)	1.4706	1.1325	48.41	48.93	15.84	15.79	36
8		95—96 (3)	1.4770	1.1402	48.60	48.64	15.48	15.79	37
9		99—100 (2)	1.4672	1.0643	58.42	58.68	13.97	13.84	45
10		110—112 (2)	1.4730	1.0807	58.17	58.38	13.93	13.84	51
11		110 (3)	1.4835	1.1538	48.73	48.64	15.89	15.79	26.7
12		124—125 (5)	1.4750	1.0886	57.93	58.38	13.74	13.84	23.5

In certain publications devoted to explaining the mechanism of isomerization of unsaturated sulfoxides [12] and systox [6], it is indicated that an ionic mechanism is preferred. In the case of unsaturated esters of thiophosphoric acid, it seems to us that there is no foundation for the postulate of an ionic mechanism, since the formation, during the isomerization of dialkyl-α-methylallylthiophosphoric ester and dialkyl-γ-methylallylthiophosphoric ester of two different isomeric O,O-dialkyl-S-methylallylthiophosphates excludes the possibility that carbonium ions can be formed as intermediate products during these reactions.

EXPERIMENTAL

The preparation of dialkyl esters of allyl- and crotylthiophosphoric acids. To the alcoholate of allyl or crotyl alcohol, prepared from 0.2-0.5 g-atom of metallic sodium and the corresponding unsaturated alcohol in 150 ml of dry benzene, there was added in small portions the calculated amount of the acid chloride of dimethyl-, diethyl- or dibutylthiophosphoric acid. The reaction took place in all cases with the evolution of heat. The reaction mixture was heated at 100° for a period of 2-3 hours. After cooling, the sodium chloride was dissolved in water, and the benzene layer was separated from the aqueous layer. The aqueous layer was extracted with ether. The ethereal extract was combined with the benzene layer, dried by means of calcium chloride, and after the distillation away of the benzene and the ether, was distilled in vacuo. The characteristics of the materials obtained are shown in the Table (numbers 1,3,5,7, and 9).

The thermal isomerization of the dialkyl esters of alkyl- and crotylthiophosphoric acids. The esters, in amounts of the order of 0.1 to 0.2 mole, were heated in a sealed tube for a period of 3-6 hours at 120-140°. The pressure at the opening of the tube was not determined. The reaction mixture was distilled in vacuo. The characteristics of the isomerized ethers are given in the Table (substances 2,4,6,8, and 10).

Interaction of the acid chloride of dimethylthiophosphoric acid with the alcoholate of methylvinylcarbinol. To the alcoholate of methylvinylcarbinol, prepared from 25 grams of methylvinylcarbinol and 5.5 grams of sodium in 150 ml benzene, was added in small portions 45 grams of the acid chloride of dimethylthiophosphoric acid. The reaction mixture was treated in the manner described above, and distilled in a vacuum. After a threefold redistillation there was obtained 5.4 grams of O,O,S-trimethylthiophosphoric ester (A), and 23.0 grams of O,O-dimethyl-S(γ-methylallyl)-thiophosphoric ester (substance 11 in the Table).

(A) B.p. 77-78° at 2.5 mm Hg; nD^{20} 1.4619; d_4^{20} 1.2128; MR_D 35.55; calculated value 35.25; % phosphorus found = 19.55; calculated = 19.85.

On heating substance 11 in a sealed tube for a period of 5 hours at 130°, it remained unchanged. Ozonolysis of the substance produced acetaldehyde, which was identified as its condensation product with dimedon (M.p. 134-136°; mixed melting point 135-136°).

Interaction of the acid chloride of diethylthiophosphoric acid with the alcoholate of methylvinylcarbinol. To the alcoholate of methylvinylcarbinol, prepared from 25 grams of methylvinylcarbinol and 5.5 grams of metallic sodium in 150 ml benzene, there was added in small portions 45 grams of the acid chloride of diethylthiophosphoric acid. The reaction mixture was treated in the manner described above, and redistilled in vacuum.

After a threefold distillation, there were obtained 11 grams of O,O-diethyl-S-ethylthiophosphoric ester [8](B), and 12.5 grams of O,O-diethyl-S(-methylallyl)-thiophosphoric ester (substance 12 in the Table).

(B) B.p. 106-107° at 5 mm Hg; nD^{20} 1.4587; d_0^0 1.1228; % phosphorus found 15.25; calculated 15.65.

Data published in the literature: B.p. 122° (20 mm Hg); d_0^0 1.1245 [5]; B.p. 122.5-123° (20 mm Hg); nD^{20} 1.4578; d_4^{20} 1.1067 [8].

The infra-red spectrum of product B gave no evidence of absorption in the region 1660-1640 cm^{-1}, which is characteristic for the double bond, and the presence of an intense absorption band with a maximum at 1263 cm^{-1} gives evidence of the presence of the thionyl structure in this product. The same intense band with an absorption maximum at 1263 cm^{-1} is also observed in the infra-red spectrum of product 12 (for which see the Table).

The effect of crotyl chloride on the sodium derivative of the diethyl ester of thiophosphoric acid. To a benzene solution of sodium diethylthiophosphate, obtained from 108 grams of diethylphosphoric acid, 18.4 grams of sodium and 25.6 grams of sulfur, was added 80 grams of crotyl chloride. The reaction mixture was heated at 80° for a period of 5 hours. After cooling, the precipitate of sodium chloride was filtered off, and the filtrate distilled in vacuo. After several redistillations there was obtained 49 grams of O,O-dimethyl-S(γ-methylallyl)-thiophosphoric ester.

B.p. 125° at 5 mm Hg; nD^{20} 1.4782; d_4^{20} 1.0890; % phosphorus found = 13.90; calculated 13.84.

The infra-red spectra of the products was determined by means of the double-ray spectrophotometer IKS-14, with resolution for wave-numbers in the range 600-1600 cm^{-1} using a sodium chloride prism, and in the range 1600-3200 cm^{-1} using a lithium chloride prism.

SUMMARY

1. A series of dialkyl esters of allyl- and crotylthiophosphoric acids has been synthesized.

2. It has been shown that the O,O-dialkyl esters of O-allyl-, O-(α-methylallyl)- and O-(γ-methylallyl)-thiophosphoric acid undergo the Claisen rearrangement on heating, with the production of the corresponding O,O,S-thiophosphoric esters. The rearrangement of O,O-dialkyl-O-(α-methylallyl)- and O,O-dialkyl-O-(γ-methylallyl)-thiophosphoric esters takes place with inversion.

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• Original Russian pagination. See C. B. Translation.

REACTIONS OF ESTERS OF ALKYLPHOSPHINIC ACIDS WITH HALOGEN-CONTAINING COMPOUNDS

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Investigations carried out in recent years have shown that deviations occur from the usual course of the Arbuzov rearrangement in the case of tin [1], silicon [2], and phosphorus halides [3]. Instead of compounds in which the phosphorus is directly linked to the element in question, phosphinic esters are obtained, in which the phosphorus is connected with the element through an oxygen atom. It is supposed that, in these reactions, a preliminary rearrangement of the phosphites into phosphinic esters takes place, these latter then reacting with the halides of tin, silicon and phosphorus (I to III below).

$$(RO)_3P \rightarrow R-\overset{\overset{O}{\|}}{P}(OR)_2$$

$$R-\overset{\overset{O}{\|}}{P}(OR)_2 + HalSnR_3 \rightarrow R-\overset{\overset{O}{\|}}{\underset{\underset{OR}{|}}{P}}-OSnR_3 + RHal \qquad (I)$$

$$R-\overset{\overset{O}{\|}}{P}(OR)_2 + Hal\overset{\overset{O}{\|}}{P}(OR)_2 \rightarrow R-\overset{\overset{O}{\|}}{\underset{\underset{OR}{|}}{P}}-O-\overset{\overset{O}{\|}}{P}(OR)_2 + RHal \qquad (III)$$

$$R-\overset{\overset{O}{\|}}{P}(OR)_2 + HalSiR_3 \rightarrow R-\overset{\overset{O}{\|}}{\underset{\underset{OR}{|}}{P}}-O-SiR_3 + RHal \qquad (II)$$

It seemed to us that it would be very interesting to elucidate the possibility of similar reactions occurring, using halogen-containing organic compounds in which the halogen-carbon bond occurs. A study of such reactions seems to be of importance also, in view of the possibility of explaining the formation of certain secondary products which sometimes arise during the carrying out of the Arbuzov rearrangement.

We commenced the investigation of this type of reaction by using alkyl halides. When the diethyl ester of ethylphosphinic acid is heated with butyl iodide at 160-165°, the evolution of ethyl iodide commenced. The reaction continued at this temperature for a period of 20 hours. The amount of ethyl iodide produced was about 85% of the theoretical quantity. When butyl bromide was used instead of the iodide, the evolution of ethyl bromide at 170-175° was, during the same period, about 62% of the theoretical quantity. Distillation of the reaction mixture in both cases led to the separation of ethylbutyl and dibutyl esters of ethylphosphinic acid. When butyl chloride was used, prolonged heating of the reaction mixture to 190° caused no observable production of ethyl chloride.

Similar results were obtained when the reactions were carried out using hexyl iodide, bromide and chloride. These reactions were performed by heating the reaction mixtures in tubes for 10 hours at a temperature of 200-210°. The results obtained are shown in Table 1.

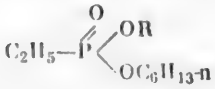
It follows from these results that the alkyl halides may be placed in the order RI > RBr> RCl, according to the reduction in reactivity for reactions with esters of alkylphosphinic acid.

TABLE 1

Alkyl halide	Yield (in %)	
	ethylhexyl ester of ethylphosphinic acid	dihexyl ester of ethylphosphinic acid
Hexyl chloride	9	0
Hexyl bromide	33	16
Hexyl iodide	33	36

TABLE 2

Alkylhexyl Esters of Ethylphosphinic Acid



Significance of R in the formula	Boiling point (pressure in mm Hg)	n_D^{20}	d_4^{20}	MR_D		Phosphorus content (%)	
				found	calculated	found	calculated
CH_3	115–117° (8)	1.4262	0.9907	53.83	54.62	14.0	14.90
C_2H_5	125–126 (7)	1.4281	0.9647	59.23	59.24	13.86	13.96
C_3H_7-n	137–138 (9)	1.4307	0.9529	64.07	63.86	13.00	13.13
C_4H_9-n	146–147 (9)	1.4320	0.9494	68.28	68.48	11.70	12.40
C_6H_{13}-n	160–162 (7)	1.4352	0.9400	77.61	77.20	—	—

In order to explain the effect on the rate of the reaction of the nature of the radicals participating in the ester group of the phosphinic ester, reactions were carried out with dimethyl, di-n-propyl and di-n-butyl esters of ethylphosphinic acid, on the one hand, and hexyl bromide on the other. It has been shown that, the greater the molecular weight of the ester radical, the higher is the temperature necessary for the commencement of the reaction (from 170° for dimethyl ester to 220° for the dibutyl ester), and the lower the yield in which the products (the alkylhexyl and dihexyl esters of ethylphosphinic acid) are obtained. When the total yield of the reaction is reduced from 90-95% in the case of the dimethyl ester to 60-65% for the dibutyl ester, the yield of the alkylhexyl ester was in all the reactions approximately twice that of the dihexyl ester. The constants for the products obtained are given in Table 2.

Reactions have also been carried out between the esters of alkylphosphinic acids and methylene iodide. These take place at 180-190°. It would be expected that the reactions could take place in three ways:

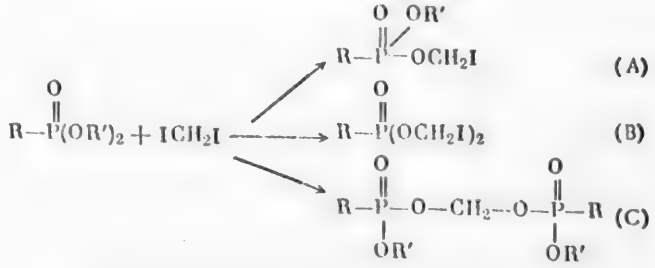
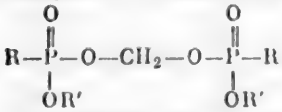


TABLE 3

Methylene-di-(alkoxyalkylphosphinic esters)



Significance in formula of		Boiling point (pressure in mm Hg)	n_D^{20}	d_4^{20}	MR_D		Phosphorus content (%)		Yield (%)
R	R′				found	calculated	found	calculated	
CH_3	C_2H_5	149—150° (8)	1.4353	1.2026	56.41	56.26	23.81	23.84	42.1
C_2H_5	C_2H_5	153—154 (9)	1.4345	1.1385	65.94	65.49	21.11	21.53	40.5
C_2H_5	C_3H_7-n	172—173 (12)	1.4320	1.0840	75.58	74.73	20.02	19.62	28.1

As a result of carrying out the reactions using the ethyl ester of methylphosphinic acid, and the ethyl and n-propyl esters of ethylphosphinic acid, there was in each case obtained only a single product, which contained no halogen. It follows that the reaction takes place according to scheme (C). The characteristics of the products obtained are given in Table 3.

The nature of all the reactions carried out is, as can be seen, limited to the exchange of one or two radicals of the ester groups of the alkylphosphinic ester for new radicals which are supplied by the alkyl iodides. These reactions may be considered as trans-alkylations. They lead to the same result as the trans-esterification reactions of esters of alkylphosphinic acid, carried out in the presence of alcohols.

The realm of trans-alkylation reactions has been further extended by us to esters of α-halogen-substituted carboxylic acids, and the halide anhydrides of carboxylic acids. The reactions of esters of alkylphosphinic acids with ethyl bromacetate takes place very smoothly, and the mono- and dicarboxyethylmethyl esters of the alkylphosphinic acids are obtained in a total yield of 80-85%. The reaction is carried out by heating to a temperature of 150-170° for 20 hours. The characteristics of the products obtained are shown in Table 4.

If the starting materials are present in equimolecular proportions, there is in all cases produced only about one half the amount of dicarboxyethylmethyl esters, compared with that of monocarboxyethylmethyl esters. It must also be noted that the temperature threshold for the commencement of the reaction diminishes gradually from 160° to 120° in passing from esters of butylphosphinic acid to those of methylphosphinic acid.

During prolonged heating of the diethyl ester of ethylphosphinic acid with the ethyl esters of α-bromopropionic acid and α-bromisobutyric acid, and also with various α-halogen esters, it appears that partial decomposition of these esters takes place, accompanied by the formation of low-boiling products and an appreciable quantity of resin. We have not succeeded in separating the individual products in the case of these reactions. It would be expected that, as a result of the reactions of the esters of alkylphosphinic acids with the acid halides of acetic and benzoic acids, the mono- and dianhydrides of phosphinic and carboxylic acids would be produced. During these reactions alkyl halides are also formed. However, the products expected are not in fact obtained. In all cases the products formed were the acid anhydrides (of acetic or benzoic acid), and esters of pyrophosphinic acid. When the experiments were carried out under uniform conditions (at a temperature of 130-140° for 8 hours) it was found that acetyl bromide produced a considerably greater yield of the pyrophosphinic ester than did acetyl chloride. The reactions evidently proceed according to the scheme:

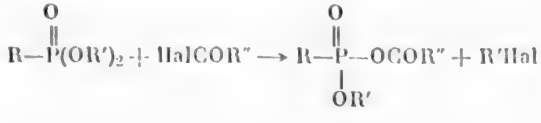
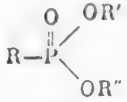


TABLE 4

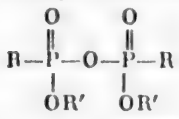
Alkylcarboxyethylmethyl and Dicarboxyethylmethyl Esters of Alkylphosphinic acids



Significance in the formula of			Boiling point (pressure in mm Hg)	n_D^{20}	d_4^{20}	MR_D		Phosphorus content (%)		Yield (%)	
R	R'	R''				found	calculated	found	calculated	individual products	total
CH_3	CH_3	$CH_2COOC_2H_5$	97—98° (1.5)	1.4310	1.2050	42.11	42.42	15.46	15.81	47	
CH_3	C_2H_5	$CH_2COOC_2H_5$	106—107 (2)	1.4360	1.1570	46.88	47.05	14.70	14.76	44	64
CH_3	$CH_2COOC_2H_5$	$CH_2COOC_2H_5$	148—148.5 (2)	1.4400	1.2120	58.29	57.93	11.68	11.56	20	
C_2H_5	C_2H_5	$CH_2COOC_2H_5$	88—89 (1)	1.4310	1.1190	51.70	51.67	13.72	13.83	40	59
C_2H_5	$CH_2COOC_2H_5$	$CH_2COOC_2H_5$	133—134 (1)	1.4390	1.1850	62.61	62.65	10.62	10.96	19	
C_3H_7-n	C_2H_5	$CH_2COOC_2H_5$	122—123 (2)	1.4320	1.1010	56.18	56.29	13.16	13.02	40	64
C_3H_7-n	$CH_2COOC_2H_5$	$CH_2COOC_2H_5$	154—155 (2)	1.4405	1.1610	67.29	67.17	10.03	10.47	24	
C_4H_9-n	C_2H_5	$CH_2COOC_2H_5$	122—123 (1)	1.4335	1.0790	60.77	60.90	12.32	12.30	37	46
C_4H_9-n	$CH_2COOC_2H_5$	$CH_2COOC_2H_5$	148—149 (1)	1.4420	1.1400	71.93	71.79	10.46	10.00	9	

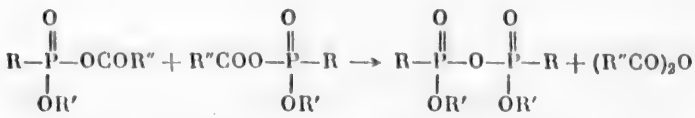
TABLE 5

Dialkyl Ester of Dialkylpyrophosphinic Acid*



No. of compound	Significance in formula of		Boiling point (pressure in mm Hg)	n_D^{20}	d_4^{20}	MR_D		Phosphorus content (%)		Yield (%)
	R	R′				found	calculated	found	calculated	
1	C_2H_5	C_2H_5	154—154.5° (9)	1.4355	1.1410	59.04	59.23	23.45	24.04	58
2	C_2H_5	C_3H_7-n.	147—149 (4)	1.4371	1.0851	69.08	68.47	21.94	21.68	24
3	C_4H_9	C_2H_5	145—146 (2)	1.4390	1.0580	77.98	77.70	19.36	19.74	25

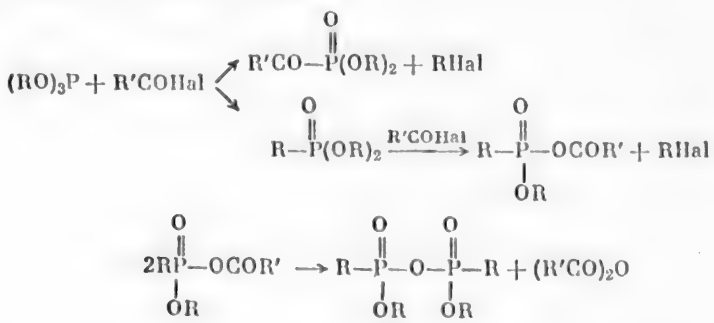
* According to data in [5], compound 1 has B.p. of 70° at a pressure of $7 \cdot 10^{-4}$ mm, and nD^{25} 1.4302.



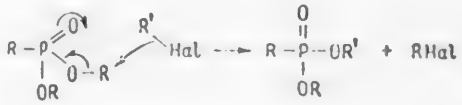
The anhydrides of carboxylic and alkylphosphinic acids produced as intermediate products undergo disproportionation with the formation of esters of pyrophosphinic acid. The characteristics of the products obtained are given in Table 5.

The anhydrides of pyrophosphinic acid, according to data in the patent literature, are also formed through the interaction of esters of alkylphosphinic acids with thionyl chloride, phosphorus oxychloride and phosphorus trichloride [4]. Certain esters of dialkylpyrophosphinic acid have been obtained earlier by the decomposition in water of the acid chlorides of alkylalkoxyphosphinic acid [5].

The results obtained by us present a clearer picture of the reaction between the acid chlorides of carboxylic acids and the fully esterified phosphorous acid. Kabachnik and Rossiiskaya [6], in a study of this reaction, have shown that the yield of ketophosphinic esters does not usually exceed 60%, and in certain individual cases, such as the reaction between triethylphosphite and acetyl chloride, only amounts to about 12%. In this case there is observed the formation of considerable quantities of high-boiling residues which were not examined more closely. When the reaction between triethyl phosphite and acetyl chloride was repeated, there was formed, in addition to the diethyl ester of acetophosphinic acid, the anhydride of pyrophosphinic acid in a yield of around 25%. It follows that the reaction in this case may take two paths:



From the results which we have obtained in the current work, it follows that, in carrying out the Arbuzov rearrangement, it is necessary to take into account the possibility that it may follow an anomalous course (with a preliminary isomerization of the phosphites into esters of the alkylphosphinic acids), not only in the case of compounds with a halogen-Sn or halogen-P bond, but also for those compounds containing the halogen-C bond. The latter reaction may occur not only with acid halides, but also with alkyl halides and more complex halogen-containing organic compounds, if the reactions are carried out at elevated temperatures and in the presence of excess of these compounds. It is still not fully clear why, when the Arbuzov reaction is carried out, there occurs in some cases a preliminary complete and facile isomerization of the phosphite esters into phosphinic esters, while in other cases the same rearrangement is either quite absent, or takes place only to a limited degree. The most probable mechanism for the reaction between the esters of alkylphosphinic acids and various halide derivatives, from our point of view, is a cyclic mechanism, which assumes the formation of intermediate, unstable, 6-membered complexes:



EXPERIMENTAL

General Method for Carrying out the Reactions. To 0.12-0.20 mole of the dialkyl ester of the alkylphosphinic acid, contained in a three-necked flask provided with a fractionating column with a descending condenser, a thermometer, and a dropping funnel, the equivalent quantity of the alkyl halide was slowly added. The flask was heated on a water bath. When the reaction mixture attained a definite temperature, the distillation commenced slowly of the alkyl halide liberated by the reaction. The course of the reaction was followed by weighing the separated alkyl halide and the reaction flask. The heating was usually continued for a period of 20-25 hours, after which the reaction mixture was distilled in vacuum, initially from the Arbuzov flask, and subsequently from a flask provided with a Vidmer or "herringbone" column. In certain cases the reaction was carried out in sealed tubes.

The Reaction Between Acetyl Bromide and the Ethyl Ester of Ethylphosphinic Acid. The reaction was performed in the way described above, using 30 grams of the ester and 22.5 grams of acetyl bromide. When the temperature of the reaction mixture reached 130-135° the distillation of ethyl bromide commenced. During 8 hours, from this, 17.2 grams of ethyl bromide were collected. Distillation of the reaction mixture gave 3.5 grams of acetic anhydride (B.p. 138-139°; n_D^{20} 1.3913; d_4^{20} 0.801), and 13.4 grams of the diethyl ester of diethylpyrophosphinic acid (see Table 5, substance 1).

When the reaction with acetyl chloride was carried out in a similar fashion, 4.6 grams of acetic anhydride and 8.4 grams of the diethyl ester of diethylpyrophosphinic acid were obtained.

The Reaction Between Benzoyl Chloride and the Ethyl Ester of Ethylphosphinic Acid. The reaction was performed using 30 grams of the ester and 25.4 grams of benzoyl chloride. The distillation of ethyl chloride commence at 145°. The temperature of the reaction mixture was subsequently raised to 170°. The reaction was carried on for a period of 10 hours. There were collected 12.3 grams of benzoic anhydride, whose B.p. was 162.5-163° at 3.5 mm Hg, and whose M.p. was 39-40° (while a mixed melting point with an authentic sample gave no depression of M.p.); and 12.6 grams of the diethyl ester of diethylpyrophosphinic acid.

SUMMARY

1. It has been shown that, on heating the esters of alkylphosphinic acids with alkyl halides, in which the radical is larger than that in the ester groups, a trans-alkylation reaction takes place. Alkyl iodides react more easily than the corresponding alkyl bromides, and these in turn more easily than the alkyl chlorides. The heavier the radical in the ester groups of the alkylphosphinic acids, the more slowly does the trans-alkylation process take place.

2. The esters of alkylphosphinic acids, when caused to react with methylene iodide, form esters of methylene-di-(alkoxyalkylphosphinic acid); while when they react with the ethyl ester of bromacetic acid they produced alkylcarboxyethylmethyl and dicarboxyethylmethyl esters of alkylphosphinic acids.

3. The result of the action between esters of alkylphosphinic acids and acid halides is the formation of dialkyl esters of dialkylphosphinic acid.

4. A suggestion is made as to the mechanism of the reactions which have been studied, and attention has been called to the necessity of taking account of them in carrying out the Arbuzov transformation.

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• Original Russian pagination. See C. B. Translation.

THE ORIENTATIONAL INFLUENCE OF SUBSTITUENTS IN THE FORMATION OF β-SUBSTITUTED PHENAZINE SALTS. IV

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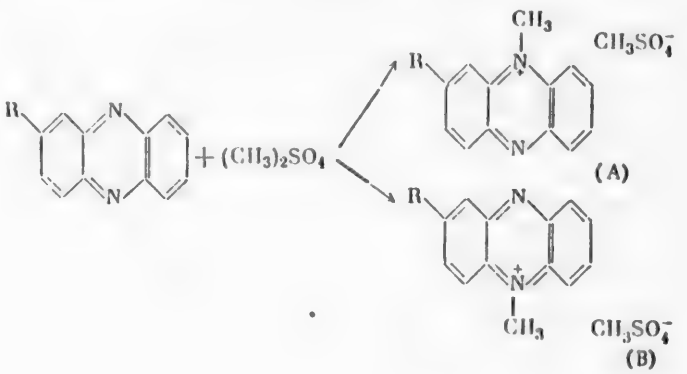
The quaternary salts of phenazine and its various substituted derivatives, which are valuable intermediate products in the synthesis of physiologically active preparations, azo dyes, analytical reagents and the like, are prepared by heating the corresponding bases of the phenazine series with dialkyl sulfates, esters of nitrobenzene sulfonic acids, or esters of n-toluene sulfonic acid. Unsubstituted phenazine, because of the uniform distribution of electronic densities between both nitrogen atoms gives only one quaternary salt. Diquaternary salts of phenazine are unknown, and can scarcely exist.

In substituted derivatives of phenazine, the electron densities of the two nitrogen atoms cease to be equivalent under the influence of electron acceptor or electron donor substituents. If such a molecule is involved in salt formation, orientational factors begin to act which modify any exclusive or preponderant direction of the reaction. In such a case, it is possible to form two isomeric quaternary salts, (A) and (B).



In the above reaction, the positive methyl ion is an electron acceptor, and the action of the alkylizing agent is directed principally toward the nitrogen atom in the unsymmetrically substituted phenazine molecule which has the greatest electron density. What is formed is practically always a mixture of two isomeric salts, the relative yield of which has so far been an unsolved problem.

The present paper describes methods and results of a study of which of the two nitrogen atoms in the phenazine ring, 9 or 10, is involved to what extent in the salt formation reaction in the presence of different substituents. For this purpose, studies were made of the spectra of bases, quaternary, mono- and diacid salts. To identify the monoacid salts, which were obtained by dissolving the corresponding bases in acid, their spectra were compared

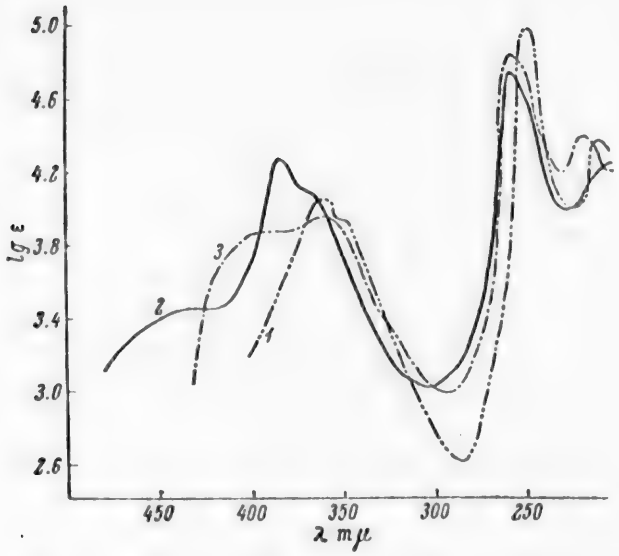
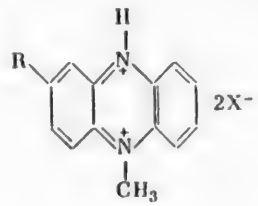


Fig. 1. 1) Phenazine, 2) perchlorate of 9-methylphenazine, 3) 2-methoxyphenazine (in alcohol).

with the spectra of similar standard quaternary salts dissolved in alcohol. The diacid salts were identified from the spectra of quaternary salts dissolved in concentrated sulfuric acid, in which the protonated quaternary salt served as the prototype of a diquaternary salt.



In some cases, binary mixtures of quaternary salts were investigated, and the amount of each component present was determined by Firordt's method [1]. Proceeding by the method described previously, standard samples of the isomeric quaternary salts [2] under investigation were prepared, along with artificial mixtures having known concentrations of each salt, and finally, mixtures of unknown composition, obtained by interaction of the base with dimethyl sulfate. The natural mixtures were treated by a standard method: after completion of the salt formation reaction, all the contaminants (base, nitrobenzene, and dimethyl sulfate) were washed out with benzene and ether. The residue of pure quaternary salt was not allowed to crystallize, in order to avoid partial or complete loss of one of the isomers. The resulting binary mixture of quaternary salts was investigated as described previously [3].

Phenazine. By allowing phenazine to react with dimethylsulfate in nitrobenzene, it is easy to get a good yield of the methylsulfate of N-methylphenazine, which is a compound that differs sharply in its physical-chemical properties from the original base. The latter is not soluble in water, but is readily soluble in benzene and toluene; the quaternary salt of phenazine, on the other hand, is very readily soluble in water, but insoluble in benzene and toluene. The phenazine and its quaternary salt have a different affinity toward nucleophilic substitution reactions. Phenazine is completely inert toward this type of reaction, while its quaternary salt reacts readily with nucleophilic agents. Because of this property, the quaternary salts of phenazine and its substituents find wide application in various fields of synthetic and pharmaceutical chemistry [4].

There are considerable differences between the absorption spectra of phenazine and its quaternary salt. The phenazine bands at 249 and 362 mμ are displaced toward the long wave length end in the quaternary salt; further,

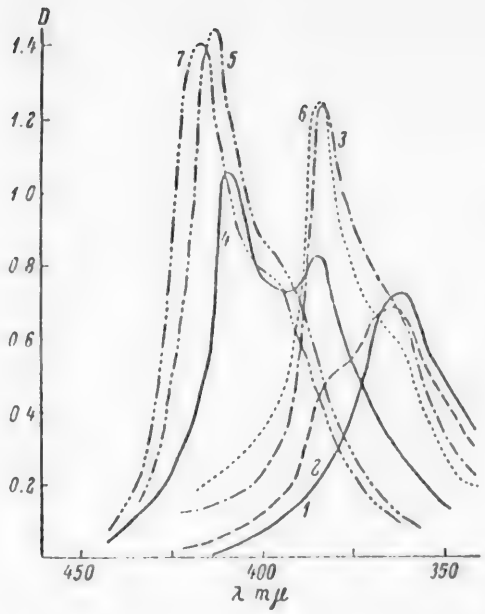


Fig. 2. 1) Phenazine in alcohol, 2) in 5% H_2SO_4, 3) in 25% H_2SO_4, 4) in 90% H_2SO_4, 5) in 96% H_2SO_4, 6) perchlorate of 9-methylphenazine in alcohol, 7) in 96% H_2SO_4. ($c = 5 \cdot 10^{-5}$ M.)

in the quaternary salt, a new band appears at the edge of the visible region. Solutions of salts of phenazine and its derivatives are more deeply colored than solutions of the bases from which they are derived. Phenazine is a weak base: its $pK_a = 1.23$ [5]. The quaternary salts of phenazine are quite stable compounds and do not hydrolyze in aqueous solution.

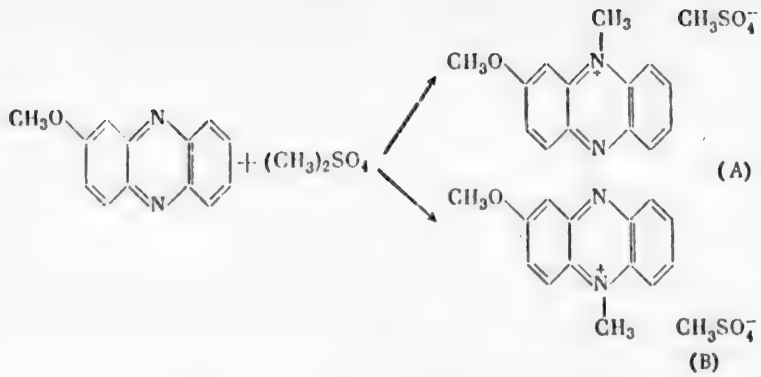
In solutions of different acid concentrations, phenazine forms mono- and diacid salts, characterized by individual absorption bands in the ultraviolet region. Consequently, the transformation of phenazine into the salt (Fig. 1, Curve 1) can be followed from the change in the absorption spectrum. In 5% sulfuric acid, diluted with alcohol, a part of the molecules of the base is protonated by the acid, and goes over into the monoacid salt. In the spectrum, this corresponds with the appearance of a hump at 380 mμ (Fig. 2, Curve 2). Increasing the acid concentration increases the concentration of the mono-salt in the solution, while the concentration of the free base decreases. Correspondingly, the molecular extinction of the mono-salt band increases, and in 25% acid it reaches its limit at E = 25,000. The quaternary salt of phenazine has the same molecular extinction in a solution of the same concentration (Fig. 2, Curves 3 and 6). This shows that in 25% acid all the base is converted into the mono-salt. If the acid concentration is raised to 75%, the protons from the acid unite with the second center of the base, namely the nitrogen atom 10, forming the diacid salt. A new band arises in the spectrum between 405 and 415 mμ. It belongs to the diacid salt of phenazine. In 90% acid, the phenazine molecules occur predominantly in the form of the di-salt. However, as can be seen from the presence of the mono-salt band in curve 4, there is a certain amount of the monoacid salt in solution. In 96% acid, the protonation of both centers of basicity in the phenazine molecule is completed (Fig. 2, Curve 5). The absorption maximum of the diacid phenazine salt lies at 413 mμ. The absorption curve of the diacid phenazine salt is similar to the absorption curve of the quaternary salt in 96% sulfuric acid (Fig. 2, Curve 7) the band maximum of which lies at 417 mμ, E = 28,400. By careful dilution of the acid solution of the phenazine salt with alcohol, it is possible to bring about alcoholysis, which can be followed from the changes in the absorption spectra, which occur in reverse order from salt formation.

Various β-substituted forms will now be discussed, in which the orientational action of the substituents is determined exclusively by the electron forces transmitted through the phenazine ring to the nitrogen atoms 9 and 10.

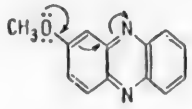
2-Methoxyphenazine. In the absorption curve of 2-methoxyphenazine, three absorption bands are distinguishable with maxima at 256, 358, and 391 mμ and E = 74,400, 9,500, and 8,000 respectively (Fig. 1, Curve 3). By heating 2-methoxyphenazine with dimethyl sulfate in nitrobenzene, it is easy to obtain a good yield of a mixture of the two quaternary salts, the methyl sulfates of 2-methoxy-9-methylphenazine (A), and 2-methoxy-10-methylphenazine (B).

The relative yield of the isomers in the mixture was determined by the spectrophotometric method. The necessary standard quaternary salts were obtained from the 9- and 10-oxides of 2-methoxyphenazine [2].

Figure 3 shows large scale segments of the absorption curves of $2 \cdot 10^{-4}$ M alcoholic solutions of the following substances: the perchlorate of 2-methoxy-10-methylphenazine (Curve 1), the perchlorate of 2-methoxy-9-methylphenazine (Curve 2), a 1:1 mixture of the two (Curve 3), the natural mixture, obtained by the action of dimethylsulfate on 2-methoxyphenazine in nitrobenzene (Curve 4). In what follows, the curves of the natural mixtures are not given in the graphs, as there is no need, for calculational purposes, to make spectrophotograms of the solution at all wavelengths. For this purpose, it is sufficient to verify whether or not all three absorption curves cross at the isobestic points, and then carry out the calculation of optical density from the pair of points found previously.

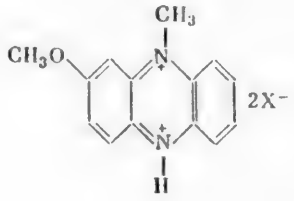


To calculate the mixtures of quaternary salts of 2-methoxyphenazine, the optical densities at wavelengths 440 and 510 mμ were used. At these points, the artificial 1 : 1 mixture of the two quaternary salts was found to contain 50.4% of one isomer, and 49.6% of the other. The data of the measurements and calculations of the natural mixtures of quaternary salts, obtained by heating 2-methoxyphenazine with dimethyl sulfate, show that 85% of the methyl sulfate of 2-methoxy-9-methyl-phenazine is formed, and 15% of the other isomer, 2-methoxy-10-methyl-phenazine.* This is easily explained in the following way. In 2-methoxyphenazine, the nitrogen atom 9 is in direct conjugation with the OCH_3-group, which sends a free pair of electrons from the oxygen atom to it through the conjugation chain.



Thus, the electron density equilibrium between nitrogen atoms 9 and 10 is shifted in favor of number 9.

In acid, 2-methoxyphenazine forms mono- and diacid salts. The monoacid salt shows an absorption band in the same region where the absorption of the two isomeric quaternary salts of 2-methoxyphenazine occurs, but in the latter case, the maxima are shifted a little toward the long wavelength end. The protonation of 2-methoxyphenazine begins in very dilute acid. Even in 0.5% acid, a certain number of the 2-methoxyphenazine molecules is converted into the monoacid salt, the absorption maximum of which lies at 385 mμ. Then with increasing acid concentration, the quantity of the salt increases correspondingly, and along with it the molar extinction of the monoacid salt band (Fig. 4, Curves 2 and 3). In 10% acid, the formation of monoacid salt is completed, with an absorption maximum at 385 mμ, E = 17,200. Judging from the fact that the band from the monoacid salt of 2-methoxyphenazine (Curve 3) lies closer to the band from the salt of 2-methoxy-9-methylphenazine (Curve 6) and is less in coincidence with the band from the salt of 2-methoxy-10-methylphenazine (Curve 5), the conclusion is reached that of the two centers of basicity in the 2-methoxyphenazine molecule, the nitrogen atom 9 is protonated first, and afterwards the protons unite with nitrogen atom 10. The diacid salt, formed in 96% acid, (Curve 4) is characterized by a large absorption band with two maxima at 420 and 440 mμ, with E = 13,000 and 14,200 respectively. That this band corresponds with the di-salt is clear from its similarity to the absorption band of the methyl sulfate of 2-methoxy-9-methylphenazine in concentrated sulfuric acid (Curve 7). In the latter case, a proton unites with the second free nitrogen atom, 10, and forms a di-salt.



* Mean of four parallel experiments.

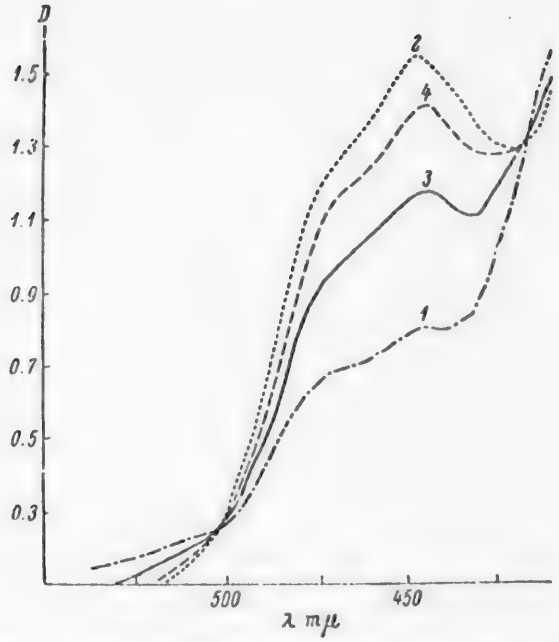


Fig. 3. Segments of absorption curves in alcohol solution ($c = 2 \cdot 10^{-4}$ M.) 1) Perchlorate of 2-methoxy-10-methylphenazine, 2) perchlorate of 2-methoxy-9-methylphenazine, 3) artificial 1:1 mixture, 4) natural mixture, obtained from the reaction of dimethyl sulfate on 2-methoxyphenazine innitrobenzene.

Comparing the spectra of 2-methoxyphenazine and unsubstituted phenazine in acid of given concentration (for example 2.5%), it is seen that phenazine does not form a salt in acid solution of this concentration, while more than half of the molecules of the 2-methoxyphenazine base go over into salt, i.e., 2-methoxyphenazine is a stronger base than unsubstituted phenazine.

2. Chlorphenazine. The absorption curve of 2-chlorphenazine coincides almost completely with the curve of unsubstituted phenazine. 2-Chlorphenazine forms two isomeric quaternary salts with dimethyl sulfate. Their relative concentration in the mixture was determined by the method described above. The optical densities at wavelengths 350 and 375 mμ were used for calculation. At these wavelengths, an artificial 50% mixture was found to contain 51.5% of one isomer, and 48.5% of the other. The data from the measurements and calculations of natural mixtures of the quaternary salts of 2-chlorphenazine forms 56% of the 2-chlor-9-methylphenazine salt, and 44% of the 2-chlor-10-methylphenazine salt. (These values are the mean of six parallel experiments). The difference in the rate of formation of the isomeric quaternary salts of 2-chlorphenazine can be explained by the properties of the chlorine atom as a substituent in an aromatic nucleus. By its I-effect, it repulses electrons from both nitrogen atoms (salt formation in 2-chlorphenazine is considerably more difficult than in unsubstituted phenazine); however, it repulses electrons less from nitrogen atom 9, with which it is conjugated, than from nitrogen atom 10. This creates the proper conditions for some preponderance of salt formation at nitrogen atom 9.

In acid, 2-chlorphenazine forms mono- and diacid salts, the spectra of which are widely different from one another. In 7.5% acid, part of the base (Fig. 5, Curve 2) goes over into the mono-salt, with a maximum at 389 mμ. The presence of a second maximum at 372 mμ shows that a part of the 2-chlorphenazine molecules is in the form of the free base. With an increase in the acid concentration (12.5%) the quantity of mono-salt in the solution increases. This can be seen from the upward displacement of the molar extinction of the salt band (Fig. 5, Curve 3). In this same region, but a little displaced toward the long wavelengths, lie the bands of the monoquaternary salts 2-chlor-9-methylphenazine, with maximum at 395 mμ, E = 20,200, and 2-chlor-10-methylphenazine,

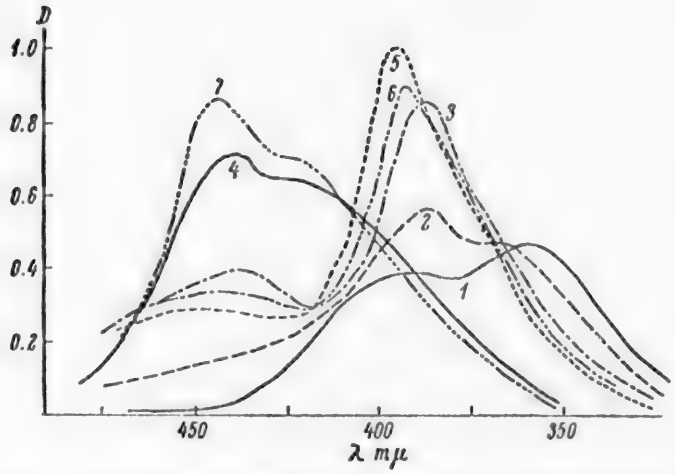


Fig. 4. 1) 2-Methoxyphenazine in alcohol, 2) in 1% H_2SO_4, 3) in 10% H_2SO_4, 4) in 96% H_2SO_4, 5) perchlorate of 2-methoxy-10-methylphenazine in alcohol, 6) perchlorate of 2-methoxy-9-methylphenazine in alcohol, 7) in 96% H_2SO_4 ($c = 5 \cdot 10^{-5}$ M.)

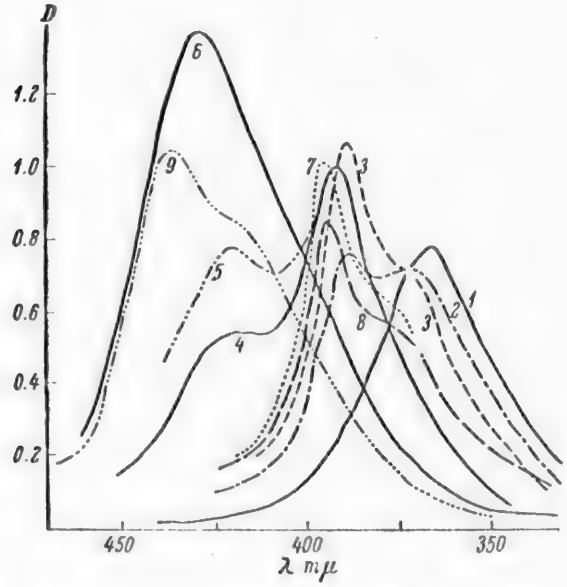


Fig. 5. 1) 2-Chlorphenazine in alcohol, 2) in 7.5% H_2SO_4, 3) in 12.5% H_2SO_4, 4) in 45% H_2SO_4, 5) in 50% H_2SO_4, 6) in 96% H_2SO_4, 7) perchlorate of 2-chlor-9-methylphenazine in alcohol, 8) perchlorate of 2-chlor-10-methylphenazine, 9) same in 96% H_2SO_4 ($c = 5 \cdot 10^{-5}$ M.)

with maximum at 391 mμ, E = 16,800 (Fig. 5, Curves 7 and 8). Proceeding from the fact that the spectrum of the monoacid salt of 2-chlorphenazine is very close to the spectra of both quaternary salts of 2-chlorphenazine, and that the presence of a substituent, as seen from the above calculations, has no great effect on the distribution

of electron densities in the phenazine ring, it can be concluded that there is no especially pronounced tendency toward preponderance in the formation of any one of the isomers of the monoacid salt in 2-chlor-phenazine. Curve 2 of Fig. 5 represents the composite absorption spectrum of the base, i.e., the monoacid salt with the proton on nitrogen atom 9, and the same salt with the proton on the other nitrogen atom. At large acid concentrations, both nitrogen atoms are subjected to proton attack. This forms the diacid salt, and a new band appears between 410 and 430 mμ. The growth in the molecular extinction of the di-salt band in Fig. 5 (Curves 4, 5, and 6) shows that with increasing acid concentration (45, 50, and 96% respectively) the di-salt concentration in the solution increases.

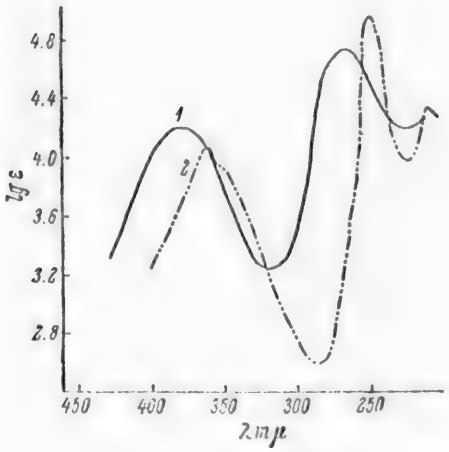
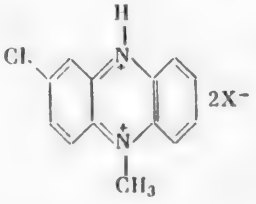


Fig. 6. 1) 2-Phenylphenazine in alcohol, 2) phenazine in alcohol.

Comparing the absorption of 2- and 1-chlorphenazines (see following communication), it is seen that in the latter, on account of steric hindrance, the di-salt is formed only in 96% acid, while in 2-chlor-phenazine, where this factor is absent, the formation of the di-salt is noticeable in the spectra even at 45% concentration. In 96% acid, judging from the form and position of the absorption curve of 2-chlorphenazine (Curve 6), the solution no longer contains either any of the free base, or any of the monoacid salt. If it is assumed that the molecular extinction of the di-salt (E = 27,200) corresponds with 100% concentration of the salt, then in 45% acid, with E = 10,800, the concentration of the di-salt is about 40%, and in 50% acid, it is about 57%. The 2-chlorphenazine di-salt band is similar to the absorption band of the perchlorate of 2-chlor-10-methylphenazine in concentrated sulfuric acid, in which it is converted into a salt of the structure:



2-Phenylphenazine. Introducing the C_6H_5 group into the phenazine ring in position 2 strongly displaces the whole phenazine curve toward the long wavelength end (Fig. 6, Curves 1 and 2). With dimethyl sulfate, 2-phenylphenazine easily gives a good yield of a mixture of the methyl sulfates of 2-phenyl-9- and 2-phenyl-10-methylphenazine. The composition of the binary mixture of the salts of 2-phenyl-9-methylphenazine and 2-phenyl-10-methylphenazine was calculated from standard curves at wavelengths of 387 and 395 mμ. At these points, the artificial 50% control mixture was found to contain 49% of the 2-phenyl-9-methylphenazine salt, and 50.2% of the 2-phenyl-10-methylphenazine salt, and for the natural mixture, obtained by the reaction of dimethyl sulfate with 2-phenylphenazine, the concentration of salt with the methyl on nitrogen atom 9 was determined to be 32%, and with the methyl on nitrogen atom 10, 68% (mean data from five parallel experiments). These data show that the basicity of nitrogen atom 9 is less than nitrogen atom 10. The reduction in basicity, and, consequently, in the salt-forming affinity of nitrogen atom 9 is to be explained, apparently, by the repulsion of electrons toward the phenyl group.

In acid, 2-phenylphenazine gives two monoacid salts, and one diacid salt, characterized by individual absorption spectra. Salt formation changes the short wavelength band at 266 mμ very little. The long wavelength band at 378 mμ is changed much more. As the base (Fig. 7, Curve 1) is converted into salt, it becomes weaker, and in high acid concentration it disappears almost completely (Fig. 7, Curve 3). Formation of mono-salt is characterized by the appearance of a new absorption band between 400 and 420 mμ (Curve 2). This is in the same place as the absorption band of the 2-phenyl-10-methylphenazine salt, which has a maximum at 408 mμ, with E = 13,600. The close resemblance of the monoacid 2-phenylphenazine salt to the perchlorate of 2-phenyl-10-

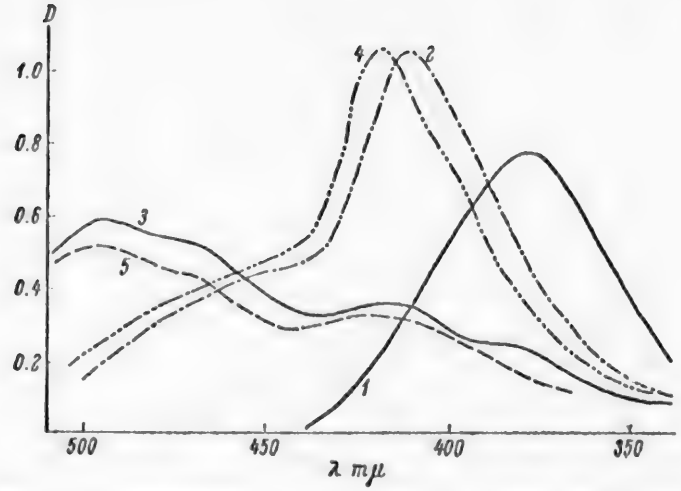


Fig. 7. 1) 2-Phenylphenazine in alcohol, 2) in 25% H_2SO_4, 3) in 96% H_2SO_4, 4) perchlorate of 2-phenyl-9-methylphenazine in alcohol, 5) perchlorate of 2-phenyl-10-methylphenazine in 96% H_2SO_4 ($c = 5 \cdot 10^{-5}$ M.)

methylphenazine, and the great difference between the former and the perchlorate of 2-phenyl-9-methylphenazine testifies in favor of the idea that 2-phenylphenazine in acid is protonized principally in position 10.

At high acid concentration, the quantity of monoacid salt in solution diminishes, and its molar extinction falls off. The mono-salt goes over into the di-salt, which makes a new band show up on the curve with a maximum at 493 mμ (Fig. 7, Curve 3). The same band occurs with the 2-phenylphenazine salt in 96% acid, to protons of which are united with the free nitrogen atom 9 or 10. In the absorption curve of 2-phenylphenazine in concentrated acid, at the places where the bands from the base (377 mμ) and the mono-salt (410 mμ) occur, small kinks remain, testifying to the fact that under these conditions, insignificant quantities of the free base and the mono-salt are present in solution.

EXPERIMENTAL

The 2-methoxyphenazine and the 2-chlorphenazine had the melting points which are given in the literature [6,7]. The remaining substances are described in earlier work [2, 8]. The technique of preparing solutions, the spectrophotometry of standards and binary mixtures of quaternary salts, as well as the calculational formulae are given in reference [3].

SUMMARY

1. The orientational influence of the substituents in the molecules of 2-methoxy-, 2-chlor-, and 2-phenylphenazine during the formation of quaternary salts by interaction with dimethyl sulfate was determined by a spectrophotometric method.

2. The formation of mono- and diacid salts of 2-methoxy-, 2-chlor-, and 2-phenylphenazine was studied in sulfuric acid solutions of various concentrations.

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SYNTHESIS IN THE PHENOTHIAZINE SERIES

IV. SYNTHESIS OF 10-β-AMINOPROPIONYL DERIVATIVES OF 2-CHLOR- AND 2-ACETYLPHENOTHIAZINE

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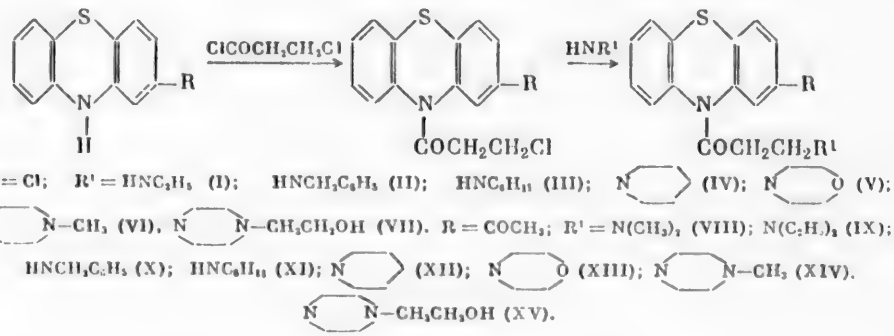
Among the dialkylaminoacyl derivatives of 2-chlorphenothiazine which we have synthesized [1], the one which has attracted the most attention from pharmacologists is 10-(β-diethylaminopropionyl)-2-chlorphenothiazine, the experimental study of which, carried out by Yu. I. Vikhlyaev and N. V. Kaverina, has shown that this compound has the specific property of dilating the coronary vessels of the heart. At the present time 10-(β-diethylaminopropionyl)-2-chlorphenothiazine hydrochloride, under the name "Khloratsizin", is being tested clinically as a therapeutic agent in certain diseases of the cardio-vascular system [2].

In the search among the aminopropionyl derivatives of phenothiazine for other active preparations having a similar action, we synthesized some new 10-β-alkylamino-, aralkylamino-, dialkylamino-, and nitrogen-containing heteroylpropionyl derivatives of 2-chlor- and 2-acetylphenothiazine. These compounds were prepared by the reaction between 2-chlorphenothiazine or 2-acetylphenothiazine and β-chlorpropionyl chloride with subsequent replacement of the chlorine in the β-chlorpropionyl group by a secondary or tertiary amino group.



R = Cl; R¹ = HNC_2H_5 (I); $HNCH_2C_6H_5$ (II); HNC_6H_{11} (III); N⟨ ⟩ (IV); N⟨ ⟩O (V); N⟨ ⟩N–CH_3 (VI), N⟨ ⟩N–CH_2CH_2OH (VII). R = $COCH_3$; R¹ = $N(CH_3)_2$ (VIII); $N(C_2H_5)_2$ (IX); $HNCH_2C_6H_5$ (X); HNC_6H_{11} (XI); N⟨ ⟩ (XII); N⟨ ⟩O (XIII); N⟨ ⟩N–CH_3 (XIV). N⟨ ⟩N–CH_2CH_2OH (XV).

In the synthesis of these compounds, we used commercially prepared 2-chlorophenothiazine. The 2-acetylphenothiazine was prepared by introducing the acetyl group into position 2 of the phenothiazine ring directly, by means of the Friedel-Crafts reaction [3]. To do this, 10-acetylphenothiazine is acetylized with acetic anhydride in CS_2 in the presence of anhydrous aluminum chloride, which gives 2,10-diacetylphenothiazine. This compound is easily hydrolyzed with alcoholic alkali to 2-acetylphenothiazine.

The reaction of β-chlorpropionylchloride on 2-chlor- or 2-acetylphenazine, under the same conditions as in the preparation of haloidacetyl derivatives of phenothiazine [4], gave an 87% yield of 10-(β-chlorpropionyl)-

2-chlorphenothiazine, and an 82% yield of 10-(β-chlorpropionyl)-2-acetylphenothiazine. Boiling the β-chlorpropionylphenothiazines in toluene solution with 2-2.5 gm.-mol. of primary or secondary amine gave 10-β-aminopropionyl substituted derivatives of 2-chlor- and 2-acetylphenothiazine which were separated in the form of the hydrochloride, the oxalate, or the tartrate.

For our pharmacological experiments we prepared hydrochlorides of the following compounds: 10-(β-ethylamino)-(I), 10-(β-piperidyl)-(IV), 10-(β-morpholyl)-(V) and 10-(β-N-methylpiperazinyl)-propionyl-2-chlorphenothiazine (VI); 10-(β-dimethylamino)-(VIII), 10-(β-diethylamino-(IX), 10-(β-piperidyl)-(XII), 10-(β-morpholyl)-(XIII), and 10-(β-N-methylpiperazinyl)-propionyl-2-acetylphenothiazine (XIV).

These substances present the appearance of small white crystals, readily soluble in water, and readily soluble in cold – but poorly in hot – alcohols (methyl, ethyl and isopropyl).

The hydrochlorides of 10-(β-benzylamino)-(II) and 10-(β-cyclohexylamino)-propionyl-2-chlorphenazine (III), 10-(β-benzylamino)-(X) and 10-(β-cyclohexylamino)-propionyl-2-acetylphenothiazine (XI), are white[except (10), which has a yellowish color], crystalline substances, difficultly soluble in water and cold alcohols (methyl, ethyl, and isopropyl), but readily soluble in hot acetone and alcohol.

The 10-{β-[4-(β'-hydroxyethyl)-piperazinyl-1]-propionyl}-2-chlorphenothiazine (VII) was separated in the form of an acid salt of oxalic acid. The 10-{β-[4-(β'-hydroxyethyl)-piperazinyl-1]-propionyl}-2-acetylphenothiazine (XV) was separated in the form of a neutral salt of tartaric acid. This was done because the hydrochlorides of these two compounds were not stable enough.

The salts recounted above are easily purified by recrystallization either from acetone or from anhydrous methyl, ethyl, or isopropyl alcohol, or from a mixture of these solvents.

Tables 1 and 2 give the properties of the salts of 10-β-aminopropionyl derivatives of 2-chlor- and 2-acetylphenazine as prepared by us.

The investigation of the substances which we synthesized was carried out in the Laboratory of Special Pharmacology of the Institute of Pharmacology and Chemotherapy of the Academy of Medical Sciences, USSR, by Yu. I. Vikhlyaev and N. V. Kaverina. The most interesting substances from the pharmacological standpoint turned out to be 10-{β-[4-(β'-hydroxyethyl)-piperazinyl-1]-propionyl}-2-chlorophenothiazine (VII) and 10-{β-[4-(β'-hydroxyethyl)-piperazinyl-1]-propionyl}-2-acetylphenothiazine (XV). These two piperazine derivatives of phenothiazine showed in the experiments that they have an effect on the coronary vessels of the heart similar to the effect of 10-(β-diethylaminopropionyl)-2-chlorphenothiazine.

EXPERIMENTAL PART

10-β-Aminopropionyl Derivatives of 2-Chlorphenothiazine

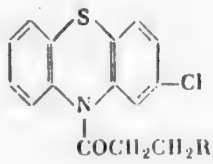
10-(β-Chlorpropionyl)-2-Chlorphenothiazine. To 117 gm. 2-chlorphenothiazine in 400 ml dry toluene add 73 gm. β-chlorpropionyl chloride dropwise and boil the reaction mixture 4 hours. Distill off the toluene and the remaining β-chlorpropionyl chloride in the vacuum from a water jet (filtration) pump. Dissolve the residue in 400 ml of anhydrous isopropyl alcohol, boil the solution for 15-20 minutes with activated charcoal, and filter. Filter off and dry the crystalline precipitate which separates out on cooling the filtrate. The yield is 140 gm. (87% of the 2-chlorphenothiazine) of a fine crystalline substance with m.p. 104-106°. Recrystallized from absolute alcohol, it melts at 111-112° (m.p. 112-113° [5]).

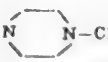
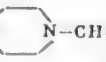
10-(β-Morpholylpropionyl)-2-Chlorphenothiazine Hydrochloride (V). Boil 8.1 gm. 10-(β-chlorpropionyl)-2-chlorphenothiazine and 4.35 gm. morpholin in 40 ml of dry toluene for 2 hours under a reflux condenser. Filter out the morpholine hydrochloride which separates on cooling, and distill off the toluene from the filtrate in vacuum. Dissolve the oily residue in dry ether, filter, and add a solution of HCl in dry ether to the filtrate. Filter off the precipitate of 10-(β-morpholylpropionyl)-2-chlorphenothiazine hydrochloride, wash with dry ether and dry in a vacuum desiccator over solid alkali. The yield is 9 gm. (87.5%) of a substance with m.p. 225°. Recrystallization from methanol did not change the melting point.

The hydrochlorides of the other aminopropionyl derivatives of 2-chlorphenothiazine were prepared in an analogous way, and their properties are given in the table.

TABLE 1

10-β-Aminopropionyl Derivatives of 2-Chlorphenothiazine

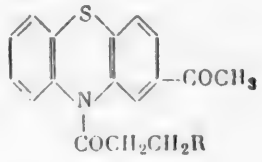


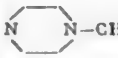
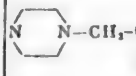
Number of substance	Meaning of R in the formula	Yield (in % of original phenothiazine)	Melting point of hydrochloride	Solvent used in recrystallizing hydrochloride	Molecular formula of hydrochloride	Analysis of hydrochloride		
						element	found %	calculated %
(I)	NHC_2H_5	—	219°	Anhydrous Ethyl Alcohol	$C_{19}H_{23}ON_2SCl_3$	Cl	19.28, 19.22	19.30
(II)	$HNCH_2C_6H_5$	79.3	201	Anhydrous Isopropyl Alcohol	$C_{23}H_{25}ON_2SCl_3$	N	6.76, 6.59	6.50
(III)	HNC_6H_{11}	92.2	222	Anhydrous Ethyl Alcohol	$C_{23}H_{31}ON_2SCl_3$	Cl	16.74, 16.43	16.75
(IV)		82.0	202	Anhydrous Isopropyl Alcohol	$C_{22}H_{31}ON_3SCl_2$	Cl	17.44, 17.21	17.63
(V)		87.5	225	Methanol	$C_{18}H_{20}O_2N_2SCl_2$	Cl	17.26	17.22
(VI)*		95.5	195—196	Anhydrous Isopropyl Alcohol	$C_{27}H_{31}ON_3SCl_3 \cdot H_2O$	N	8.95, 8.90	8.85
(VII)*		90.0	184—185	Methanol	$C_{21}H_{25}O_6N_3SCl$	Cl N	5.94, 6.05 7.23, 7.51	6.00 7.04

*(VI) — separated and confirmed analytically in the form of the dihydrochloride with a molecule of water; (VII) — acid oxalate.

TABLE 2

10-β-Aminopropionyl Derivatives of 2-Acetylphenothiazine



Number of substance	Meaning of R in the Formula	Yield (in % of original phenothiazine)	Melting point of hydrochloride	Solvent used in recrystallizing hydrochloride	Molecular formula of Hydrochloride	Analysis of hydrochloride		
						element	found %	calculated %
(VIII)	$N(CH_3)_2$	83.2	202—203°	Anhydrous Ethyl Alcohol	$C_{19}H_{21}O_2N_3SCl$	Cl	9.63, 9.83	9.45
						N	7.42, 7.37	7.47
(IX)	$N(C_2H_5)_2$	89.0	159—160	Anhydrous Isopropyl Alcohol	$C_{21}H_{25}O_2N_3SCl$	Cl	8.83, 8.54	8.72
						—	—	—
(X)	$HNCH_2C_6H_5$	55.0	90 Illegible	Anhydrous Isopropyl Alcohol	$C_{24}H_{23}O_2N_3SCl$	Cl	8.10, 8.06	8.12
						—	—	—
(XI)	HNC_6H_{11}	70.0	187	Benzene and Ether	$C_{24}H_{27}O_2N_3SCl$	Cl	8.25, 8.35	8.25
						N	6.59, 6.82	6.50
(XII)		95.0	172—173	Ethyl Alcohol	$C_{24}H_{25}O_2N_3SCl$	Cl	8.37, 8.25	8.52
						—	—	—
(XIII)		Quantitative	192—193	Ethyl Alcohol	$C_{24}H_{25}O_3N_3SCl$	Cl	8.36, 8.59	8.49
						—	—	—
(XIV)*		90.0	201—202	Anhydrous Isopropyl Alcohol	$C_{23}H_{27}O_2N_5SCl_2$	Cl	14.45, 14.46	14.57
						N	8.46, 8.36	8.64
(XV)*		87.2	75 (With separation)	Acetone	$C_{27}H_{33}O_9N_3S$	N	7.36, 7.44	7.30

*(XIV) — separated and confirmed analytically in the form of the dihydrochloride with a molecule of water; (XV) — neutral tartrate.

10-β-Aminopropionyl Derivatives of 2-Acetylphenothiazine

2-Acetylphenothiazine. Add 14.2 ml of acetic anhydride over the course of 30-40 minutes at 20-22° to 30 gm. of 10-acetyl phenothiazine and 67 gm. anhydrous aluminum chloride in 300 ml dry CS_2, and boil the mixture for 7 hours. After the mixture has cooled, pour off the CS_2, and decompose the sticky residue with ice and hydrochloric acid. Extract the solution three times with ether using 200 ml portions. Wash the ether extract first with dilute hydrochloric acid, then with a solution of soda in water, dry with sodium sulfate, and distill off the ether. The greasy yellow residue solidifies on rubbing. The yield is 50 gm. of 2,10-diacetylphenothiazine, which by hydrolysis with an alcoholic solution of caustic potash gives 25 gm. of 2-acetylphenothiazine with m.p. 183°. Recrystallized from ethyl acetate, it melts at 191-192° (m.p. 193 [3]).

10-(β-Chlorpropionyl)-2-Acetylphenothiazine. Boil 15 gm. 2-acetylphenothiazine and 13 gm. β-chlorpropionyl chloride in 100 ml of anhydrous toluene for 2 hours under a reflux condenser. Filter out and dry the yellow crystalline mass that separates on cooling. The yield is 17 gm. (82% of the 2-acetylphenothiazine) of a substance with m.p. 139-140°, which after recrystallization from anhydrous isopropyl alcohol melts at 146-147°. The yellowish-colored prisms (from anhydrous isopropyl alcohol) are readily soluble in hot acetone, alcohol and toluene. They are insoluble in water.

Found %: N 4.34, 4.61; Cl 10.81, 10.69. $C_{17}H_{14}O_2NSCl$. Calculated %: N 4.22; Cl 10.62.

10-{β-[4-(β'-Hydroxyethyl)-Piperazinyl-1]-Propionyl}-2-Acetylphenothiazine Tartrate (Neutral Salt) (XV). Boil 1.65 gm. 10-(β-chlorpropionyl)-2-acetylphenothiazine and 1.3 gm. N-(β-hydroxyethyl)-piperazine in 25 ml of anhydrous toluene for 2.5 hours under a reflux condenser. Filter out the N-(β-hydroxyethyl)-piperazine hydrochloride, and distill the toluene out of the filtrate. Dissolve the residue in absolute alcohol, and add an alcoholic solution of tartaric acid. Filter off and dry the precipitate. The yield is 2.5 gm. of a fine crystalline substance which, after two recrystallizations from methanol, melts at 75°. The substance is readily soluble in water, moderately soluble in hot methyl and ethyl alcohol, and insoluble in acetone.

10-(β-Diethylaminopropionyl)-2-Acetylphenothiazine Hydrochloride (IX). Boil 1.65 gm. 10-(β-chlorpropionyl)-2-acetylphenothiazine and 0.73 gm. of diethylamine for two hours under a reflux condenser. After separating the diethylamine hydrochloride and distilling off the toluene, dissolve the residue in dry ether, and saturate the ether solution with dry hydrogen chloride. Filter off the precipitated hydrochloride, wash with dry ether and dry. The yield is 1.8 gm (89%), m.p. 135-136°. Recrystallized from acetone, and then from anhydrous isopropyl alcohol, it melts at 159-160°. Colorless, small crystals, readily soluble in water, hot acetone, ethyl and isopropyl alcohol.

The other hydrochlorides of the β-aminopropionyl derivatives of 2-acetylphenothiazine were prepared in the same way, and their properties are given in Table 2.

SUMMARY

New 10-β-aminopropionyl derivatives of 2-chlorphenothiazine and 2-acetylphenothiazine were prepared.

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*Original Russian pagination. See C. B. Translation.

THE MECHANISM OF REGROUPING IN N-NITROAMINES

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The regrouping of N-nitroamines in acid media into o- and p-nitroamines, studied by Bamberger and others [1-8], has long attracted the attention of chemists. In studying the mechanism, they have tried to clear up the question of whether the regrouping proceeds by way of the displacement of a nitro group into the ortho position inside a single molecule, or whether it is by way of acid hydrolysis of the nitroamine, with subsequent nitration of other molecules in the ortho position by the nitric acid which is formed. In the latter case, the nitrating agent ought to be detectable in the reacting medium.

Comparison of the relationships among the ortho, meta, and para isomers in the regrouping of phenylnitroamine and the nitration of aniline [6, 8], as well as other investigations, have shown that these two processes proceed independently of one another. The nitrating agent does not appear in the reacting medium in the regrouping, which, consequently, is taking place intra-molecularly. In some cases, partial denitration occurs, but it bears no relation to the ortho regrouping. On the basis of material collected from the literature, Ingold [9] accepts the intra-molecular mechanism, and proposes a scheme for the regrouping.

Recently, Brownstein and his co-workers [10] have shown that in the regrouping of phenylnitroamine in 74% sulfuric acid at -20° in the presence of $KN^{15}O_3$ the o- and p-nitroanilines formed have the normal isotopic constitution of nitrogen. This shows that the ortho- and para-regrouping can not be proceeding inter-molecularly, as this would involve the nitrating agent in the surrounding medium. The authors concluded from this that the regrouping proceeds intra-molecularly and they accordingly extended Ingold's scheme to the formation of the para-isomer.

It is possible, however, to imagine an inter-molecular mechanism in which it is not necessary to have a nitrating agent in the reacting medium participating in the process. This can take place in the case that two molecules of N-nitroamine form an intermediate complex, in which the nitro-group is transferred from one molecule to the other. The results obtained till the present time give the same amount of support both to the intra-molecular mechanism and to an inter-molecular mechanism of this sort.

To verify the possibility of an inter-molecular mechanism, we carried out a combined regrouping of phenylnitroamine, containing 9.1% N^{15} in the nitro group, with ordinary p-tolylnitroamine. With the intra-molecular mechanism, the m-nitro-p-toluidine would show the natural content of 0.37% N^{15}. In the case of the inter-molecular mechanism, it would contain 1.82% N^{15}.* Actually, 0.45-0.60% N^{15} was found in the m-nitro-p-toluidine. Taking account of the possibility of contamination of the m-nitro-p-acetamino benzoic acid with marked products

* This value is calculated from $(0.37 \cdot 5 + 9.1)/6$, as two thirds of the m-nitro-p-toluidine remains light, and one third becomes half heavy with the nitrogen atom from the phenylnitroamine. This is correct from the statistical distribution of all the colliding molecules, which is what we assumed.

(see below), this value can be considered close to the natural N^{15} content. Consequently, these results allow us to reject any sort of intermolecular mechanism for the nitroamine regrouping and to assume that it proceeds intramolecularly.

The investigation was carried out in the following way. Phenylnitroamine-$N^{15}O_2$ and p-tolylnitroamine, prepared as in references [1-3 and 11] (1 : 1 molar ratio), were dissolved in ether, and mixed with concentrated hydrochloric acid at 0°. After several hours, the products of the regrouping separated by steam distillation (the p-nitroaniline does not go over) and oxidation of the acetylized o-nitroaniline and m-nitro-p-toluidine with potassium permanganate. The m-nitro-p-acetaminobenzoic acid separated in this way, in spite of recrystallization, was apt to contain o-nitroacetanilide-N^{15}, which raised its N^{15} content. The acid from various experiments had m.p. 207-213° (220-221° in the literature).

The o- and p-anilines could not be separated in the pure state by this method, therefore their N^{15} content is uninformative, and is not given here.

SUMMARY

It is shown that in a combined regrouping of phenylnitroamine-$N^{15}O_2$ with p-tolylnitroamine, the heavy nitrogen does not enter into the product of the reaction, m-nitro-p-toluidine. This excludes the possibility of an inter-molecular mechanism in nitromaine regrouping.

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REACTION OF KETONES WITH AMMONIACAL SOLUTION OF SILVER OXIDE

III. OXIDATION OF DESOXYBENZOIN

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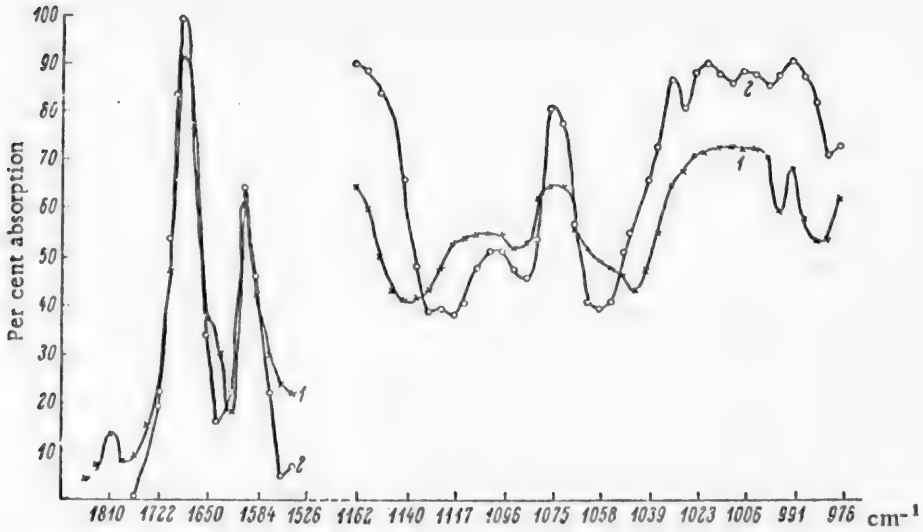
As was shown previously, aliphatic-aromatic ketones of the general formula $ArCH_2COR$ are readily oxidized by ammoniacal silver oxide solution [1, 2]. With the aim of obtaining data on the substances which are formed in this reaction, in the present work a study was made of the oxidation of desoxybenzoin (phenyl benzyl ketone, further designated as PBK). In contrast to the ketones studied earlier [1, 2], PBK in the cold is oxidized very slowly; the reaction goes well only at a temperature near to the melting point of PBK (in the order of 55°).

As a result of the reaction of PBK with Ag_2O there are formed metallic silver, a small amount of benzoic acid (about 10% of the weight of the PBK), and a neutral solid product which was separated by solvent treatment into three substances: (I) soluble in ether and hot alcohol, yellow color (~55%); (II) soluble in ether but insoluble in alcohol, light-yellow (~25%); (III) insoluble in ether, white (~20%). Analysis demonstrated that the substances (I-III) have approximately the same molecular weight and content of carbon and hydrogen; their composition may be represented approximately by the formula $C_{56}H_{42}O_5$.

Judging by the analytical data, the substances which we obtained are not reported in the literature as products of the condensation conversions of PBK studied by N. N. Zinin and subsequent investigators [3], namely: benzylidene-bis-desoxybenzoin (benzamarone) $[C_6H_5COCH(C_6H_5)]_2CHC_6H_5$ [4], bidesyl [dibenzoyldibenzyl] $[C_6H_5COCH(C_6H_5)]_2$ [5], phenyl benzyl carbinol [6], desoxybenzoinpinacone [7], and also benzil (dibenzoyl) and benzoin. The absence of the latter substances was shown by qualitative reactions [8]. In view of the insolubility of substances (I-III) in caustic under the conditions of experiment, they are not acids of the amaric acid type [6], nor are they lactones or esters, the formation of which has been noted in the oxidation of aliphatic-aromatic ketones by hydrogen peroxide [9].

For clarifying the structure of the substance (I), the 2,4-dinitrophenylhydrazone was obtained; according to the analysis this represents a derivative of a monocarbonyl compound of the above-indicated formula $C_{56}H_{42}O_5$. A study of the infrared spectra of substances (I) and (III) confirmed the presence of the carbonyl group (absorption peaks at 1684 and 1669 cm^{-1} respectively) [10]; an analogous peak is found in the spectrum of the original PBK (see figure). The absence of characteristic peaks in the region of 980-1160 cm^{-1} in the spectrum of substance (I) indicates the absence of the C-O-C ether group [10].

On the basis of these facts, it can be concluded that in the action of Ag_2O on PBK there apparently are formed aryl ketones—the products of condensing four molecules of PBK. At present we have not conducted a more detailed investigation of the structure of these substances.



Infrared absorption spectra. 1) Oxidation product (I); 2) desoxybenzoin.

EXPERIMENTAL

PBK was obtained by dry distillation of benzoin with zinc dust [11]. M.p. 56-57° (from methanol); literature data m.p. 55-56° [12], 57° [13], 52-58° [14], 59-60° [15]. The yield of recrystallized PBK in our experiments was 20-30%; nevertheless, the given method should be considered as very convenient for the small-scale preparation of PBK because of its extreme simplicity.

Oxidation of PBK. A solution was made up from 0.078 g-mole silver oxide in ~0.7 g-mol of aqueous ammonia, 6.5 g NaOH, and water to a total of 500 ml. This oxidizing mixture was heated to 54°, and 7 g (0.0357 g-mole) of PBK (dissolved in 50 ml alcohol) was added dropwise with stirring. The PBK addition was completed in 2 hours, after which heating and mixing were continued for 2.5 hours more; at this time the reaction was practically complete, as evidenced by the constancy of the quantity of silver in the solution. The total consumption of silver oxide was 0.072 g-mole, i.e., 2 g-moles of Ag_2O per g-mole of PBK.

Separation of Reaction Products. The metallic silver and the solid organic substances were filtered off from the alkaline solution. From the solution, 0.8 g of benzoic acid was recovered. The sediment was washed with cold alcohol and then was treated several times with acetone. The material remaining on the filter was metallic silver (confirmed by analysis). After evaporation of the acetone, 5.95 g of a yellow-orange crystalline product was obtained. This product was treated with ether on a filter; from 1 g there remained 0.17 g of the ether-insoluble substance (III), which was white in color. After evaporation of the ether there was formed a yellow viscous substance, which was gradually converted upon standing in air (or converted in a few hours in a vacuum desiccator) to a glassy mass, very readily crushed to a powder. Upon treatment with hot alcohol, about 2/3 was dissolved, leaving a light-yellow substance (II), insoluble in alcohol; after evaporating off the alcohol solution, yellow crystals of the substance (I) were obtained. For purification, (I) was recrystallized from ethanol, (II) from isopropanol, and (III) from ethyl acetate; prior to analysis they were dried in vacuum at 50°. Substances (I-III) are readily soluble in benzene, chloroform, and dioxane. They have indistinct melting points, over a wide temperature range: (I) 96-105°, (II) 130-137°, (III) 195-205°.

Analytical data. (I). Found %: C 84.40, 84.32; H 5.51, 5.62. M 793 (benzene). (II). Found %: C 84.91, 84.94; H 5.52, 5.41, M 787, 771. (III). Found %: C 84.52, 84.69; H 5.51, 5.31. M 781. $C_{56}H_{42}O_5$. Calculated %: C 84.60; H 5.33. M 794.3.

The 2,4-dinitrophenylhydrazone of substance (I) was obtained in the usual manner [16]. The product was dissolved in ether, the ether was evaporated, and the residue was recrystallized from anhydrous alcohol; m.p. 140-148° (indistinct).

Found %: N 6.32, 6.29. $C_{42}H_{46}O_8N_4$. Calculated %: N 5.75.

The infrared spectra were taken* on an IKS-11 spectrograph with NaCl prism, the PBK and (I) in solution in CCl_4 and the (III) in suspension in white oil.

SUMMARY

By oxidation of desoxybenzoin by caustic ammoniacal solution of silver oxide at 54°, a mixture of carbonyl-containing compounds is formed, approximating the composition $C_{55}H_{42}O_5$, and also a small quantity of benzoic acid.

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* The spectra were taken in the laboratory of Leningrad State University by O. V. Sverdlova, to whom I express deep gratitude.

CYANINE DYES WITH UNSATURATED SUBSTITUENTS

VII. THIACYANINES CONTAING β-CYANOVINYL RADICALS ON THE BENZOTHIAZOLE RINGS

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Previously we had obtained thiacyanine dyes containing unsaturated substituents in the 5,5'- and 6,6'-positions of the benzothiazole rings [1]. A study of the optical properties of these dyes showed that the introduction of unsaturated groups into the benzothiazole rings displaces the absorption band sharply toward the long-wave region of the spectrum.

In the present communication, information is given on cyanine dyes containing β-cyanovinyl radicals on the benzothiazole and quinoline rings. New bases were obtained by the Meerwein reaction [2] by the interaction of acrylonitrile with diazonium salts obtained from 2-methyl-5-amino- and 2-methyl-6-aminobenzothiazole and 6-aminoquinaldine [2-methyl-6-aminoquinoline].

Arylation and haloarylation* of the nitriles of α-β-unsaturated acids have been studied only for two representatives – the nitrile of cinnamic acid, and acrylonitrile. Meerwein [2] showed that the nitrile of cinnamic acid reacts readily with p-chlorobenzenediazonium chloride, forming α-(p-chlorophenyl)-cinnamic acid.

$$C_6H_5-CH=CH-CN + p\text{-}ClC_6H_4\overset{+}{N}_2\bar{C}l \rightarrow C_6H_5-CH=\underset{\displaystyle C_6H_4Cl\text{-}p}{\underset{|}{C}}-CN + N_2 + HCl$$

The haloarylation of acrylonitrile has been studied in very great detail [5-9]. The interaction of acrylonitrile with diazonium salts was first described by Coelsch [5], who showed that an aryl diazonium chloride under the conditions of the Meerwein reaction forms the corresponding α-chloro-β-arylpropionitrile:

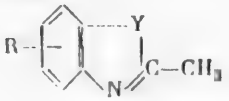
$$CH_2=CH-CN + Ar\overset{+}{N}_2\bar{C}l \rightarrow Ar-CH_2-\underset{\displaystyle Cl}{\underset{|}{CH}}-CN + N_2$$

As a rule, in this reaction the halogen adds to the α-carbon atom, and the aromatic radical to the β-carbon atom.

*A. B. Dombrovskii [3, 4] has proposed the name "haloarylation" for the reaction between unsaturated compounds and aryldiazonium halides, as a result of which the aromatic radical and the halogen atom of the diazo compound add to the multiple carbon–carbon bond.

TABLE 1

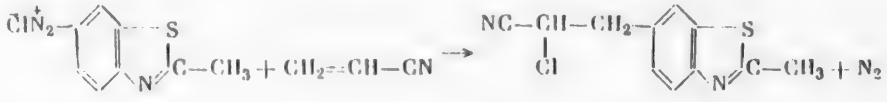
Bases



Compound No.	R	Y	Position of substituent R	Yield, %
(I)	NC—CH(Cl)—CH_2—	S	6	46
(II)	NC—CH(Cl)—CH_2—	S	5	50
(III)	NC—CH=CH—	S	6	65
(IV)	NC—CH=CH—	S	5	60
(V)	NC—CH=CH—	—CH=CH—	6	48

In studying the reaction of haloarylation of acrylonitrile, it was established [9] that it is necessary to maintain a definite temperature range and pH of the medium, depending on the nature of the aromatic compound.

Up to the present, diazo compounds of the heterocyclic series had not been reacted with acrylonitrile. By reacting diazotized 2-methyl-5-aminobenzothiazole, 2-methyl-6-aminobenzothiazole, and 2-methyl-6-aminoquinoline with acrylonitrile, bases were obtained as shown in Table 1 (substances I, II).



It was found that the chloropropionitriles which we synthesized are very stable compounds, which only upon heating in quinoline to 180° split off hydrogen chloride and are converted to 2-methyl-β-cyanovinylbenzothiazoles (substances III and IV).

The bases shown in Table 1 were converted to quaternary salts, and the latter were converted to cyanine dyes.

Tables 2 and 3 show the absorption peaks of the carbocyanines, thiadicarbocyanines, and dimethinemerocyanines which we obtained, and also for comparison the absorption peaks of the corresponding styryl derivatives which we had obtained previously [1].

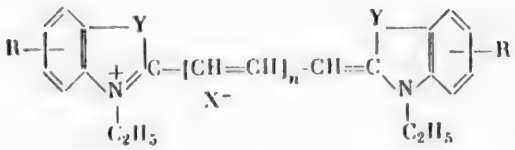
From the data of Table 2 it follows that the introduction of the β-cyanovinyl radical into the carbocyanine molecule gives rise to an 11-14 mμ shift of the absorption peak toward the long-wave region of the spectrum. It is interesting that the absorption peaks of the thiacarbocyanines containing styryl and β-cyanovinyl radicals in the 6,6'-position are almost identical, and the absorption curves are of the same type throughout.

The nitrile group, being a strongly electronegative substituent, in conjunction with the double bond, gives rise to a drawing of electrons from the benzothiazole ring and the polymethine chain, as a result of which the chromophore is lengthened, which contributes to deepening the color.

Upon introduction of unsaturated radicals into the 5,5'- and 6,6'-position of thiadicarbocyanines (Table 2) there is also observed a significant shift of the absorption peak toward the long-wave region of the spectrum, a greater bathochromic effect occurring for the 6,6'-derivatives than for 5,5'-derivatives. This is probably connected

TABLE 2

Carbocyanines and Thiacarboxyanines



Compound No.	R	n	Y	Position of substituent R	Absorption peak, mμ	Displacement of absorption peak, mμ, in comparison with (A)
(A)	H	1	S	—	559	—
—	C_6H_5—CH=CH—	1	S	6,6′	596	+37
(VI)	NC—CH=CH—	1	S	6,6′	594	+35
—	C_6H_5—CH=CH—	1	S	5,5′	578	+19
(VII)	NC—CH=CH—	1	S	5,5′	570	+11
(A)	H	1	—CH=CH—	—	607	—
—	C_6H_5—CH=CH—	1	—CH=CH—	6,6′	645	+38
(VIII)	NC—CH=CH—	1	—CH=CH—	6,6′	640	+33
(A)	H	2	S	—	650 [10]	—
(IX)	C_6H_5—CH=CH—	2	S	6,6′	694	+44
(X)	NC—CH=CH—	2	S	6,6′	689	+39
(XI)	C_6H_5—CH=CH	2	S	5,5′	676	+26
(XII)	NC—CH=CH—	2	S	5,5′	667	+17

with the fact that the conjugation of the unsaturated substituents with the polymethine chromophore is much better accomplished through the nitrogen atom of the benzothiazole ring than through the sulfur atom.

Table 3 shows absorption peaks of the dimethinemerocyanines. It was found that the introduction of the cyanovinyl radical into the 6-position of the merocyanine molecule gives rise to a shift of the absorption peak toward greater wavelength, but somewhat less than the shift given by the introduction of the styryl group. Upon introduction of the cyanovinyl group into the 5-position of the merocyanine, the absorption peak is completely unchanged. Previously E. D. Sych had found [11] that 3,3'-diethyl-5,5'-dinitrothiacarbocyanine has an absorption peak at 560 mμ, while 6,6'-dinitrothiacarbocyanine absorbs at 585 mμ.

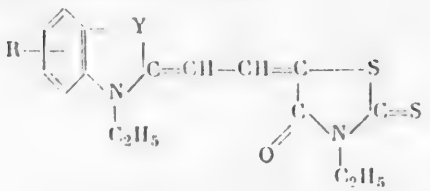
In the synthesis of the quaternary salts and dyes from 2-methyl-(β-cyano-β-chloroethyl)-benzothiazoles we noted that upon heating of the bases and the ethyl ester of p-toluenesulfonic acid to 135-140°, a partial separation of hydrogen chloride was already observed. Upon condensing this quaternary salt with orthoformic ester in pyridine, 6,6'-di-β-cyanovinylthiacarbocyanine is formed exclusively.

The quaternary salts of 2-methyl-(β-cyano-β-chloroethyl)-benzothiazoles are obtained only by short-time heating of the bases with diethyl sulfate in a water bath. With gentle heating of the indicated quaternary salts with orthoformic ester in acetic anhydride, there are formed thiacarbocyanines with absorption peaks: 566 mμ for 6,6'- and 564 mμ for 5,5'-substituted.

The cationic charge on the benzothiazole ring which arises upon alkylation of the bases increases the negative character of the benzothiazole ring. Apparently this results in easier dehydrochlorination and double bond formation.

TABLE 3

Dimethinemerocyanines



Compound No.	R	Y	Position of substituent R	Absorption peak, mμ	Displacement of absorption peak, mμ, in comparison with (A)
(A)	H	S	—	524	—
--	C_6H_5 CH=CH—	S	6	540	+16
(XIII)	NC—CH=CH—	S	6	535	+11
-	C_6H_5—CH=CH—	S	5	531	+ 7
(XIV)	NC CH=CH—	S	5	524	0
(A)	H	—CH=CH—	—	568	—
-	C_6H_5—CH=CH—	—CH=CH—	6	584	+16
(XV)	NC—CH=CH—	CH=CH—	6	580	+12

Alcoholic solutions of thiacarbocyanines and thiadicarbocyanines containing β-cyanovinyl radicals are very strongly fluorescent. Upon the introduction of alkyl groups into position 9 of the thiacarbocyanines, the fluorescence disappears completely.

EXPERIMENTAL

2-Methyl-5-aminobenzothiazole [12], 2-methyl-6-aminobenzothiazole [13], and 2-methyl-6-aminoquinoline [13] were prepared by methods developed earlier.

2-Methyl-6-(β-cyano-β-chloroethyl)-benzothiazole (I). A mixture of 100 ml acetone, 5.3 g (0.1 g-mole) acrylonitrile, and 24 g crystalline sodium acetate in a three-necked flask was cooled to -15°. 16.4 g (0.1 g-mole) 2-methyl-6-aminobenzothiazole was dissolved in 25 ml concentrated hydrochloric acid and 20 ml water. The solution was cooled to -5 to -8° and diazotized with 7.5 g sodium nitrite in 12 ml water. After standing for 5 minutes in the cooling mixture, the diazonium chloride was added in one lot to the contents of the flask; then a solution of 5.2 g cupric chloride in 10 ml water was added. The reaction mixture was stirred 2 hours at -2°, then two hours more while slowly warming to room temperature. Stirring was continued 4 hours at room temperature. Then the mixture was transferred to a distilling flask, and the acetone, chloroacetone, and 2-methyl-6-chlorobenzothiazole were removed by steam distillation. About 2.5 liters of distillate was collected. A dark-brown oil remained in the flask; this along with the water was poured into a beaker. On the following day a solidified lump was separated from the water layer, pulverized, and dried. Weight 22 g. The residue was then dissolved in hot chloroform, the solution was filtered, and the insoluble part of the residue (5 g) was washed on the filter. The solution after partial distillation of the chloroform was subjected to chromatography on aluminum oxide. The chloroform was distilled from the eluate. A dark oil was obtained, which was dissolved in benzene and again subjected to chromatography. Benzene was used as eluent. A viscous light-yellow oil was obtained, which began to crystallize after one day. Yield 10.9 g (46%), m.p. 57-59°. Six experiments were conducted on synthesis of the base. Increasing the charge did not reduce the yield, which averaged 44.3%. Part of the base was vacuum distilled at 168-169° (4 mm). There was obtained a colorless, viscous oil, which crystallized upon stirring. Colorless crystals, m.p. 71-73°.

TABLE 4

Compound No.	Name of dye	Solvent for crystallization
(VI)	3,3'-Diethyl-6,6'-di-(β-cyanovinyl)-thiacarbocyanine ethyl p-toluenesulfonate	Alcohol
(XVI)	3,3'-Diethyl-9-methyl-6,6'-di(β-cyanovinyl)-thiacarbocyanine ethyl p-toluenesulfonate	The same
(XVII)	3,3',9-Triethyl-6,6'-di-(β-cyanovinyl)-thiacarbocyanine ethyl p-toluenesulfonate	"
(VII)	3,3'-Diethyl-5,5'-di-(β-cyanovinyl)-thiacarbocyanine ethyl p-toluenesulfonate	Glycol (75 ml)
(XVIII)	3,3'-Diethyl-9-methyl-5,5'-di-(β-cyanovinyl)-thiacarbocyanine ethyl p-toluenesulfonate	Glycol (60 ml)
(XIX)	3,3',9-Triethyl-5,5'-di-(β-cyanovinyl)-thiacarbocyanine ethyl p-toluenesulfonate	Pyridine
(VIII)	1,1'-Diethyl-6,6'-di-(β-cyanovinyl)-quinocarbocyanine ethyl p-toluenesulfonate	Alcohol
(X)	3,3'-Diethyl-6,6'-di-(β-cyanovinyl)-thiacarbocyanines ethyl o-toluenesulfonate	Pyridine
(XII)	3,3'-Diethyl-5,5'-di-(β-cyanovinyl)-thiadicarbocyanine ethyl p-toluenesulfonate	The same
(IX)	3,3'-Diethyl-6,6'-distyrylthiadicarbocyanine bromide	"
(XI)	3,3'-Diethyl-5,5'-distyrylthiadicarbocyanine bromide	"
(XIII)	3-Ethyl-5-(3'-ethyl-6'-β-cyanovinylbenzothiazolenylidene-2'-ethylidene)-thiazolidine-thione-2-one-4	Pyridine–alcohol
(XIV)	3-Ethyl-5-(3'-ethyl-5'-β-cyanovinylbenzothiazolenylidene-2'-ethylidene)-thiazolidine-thione-2-one-4	Pyridine
(XV)	3-Ethyl-5-(1'-ethyl-6'-β-cyanovinyldihydroquinolylidene-2'-ethylidene)-thiazolidine-thione-2-one-4	Pyridine–benzene

Found %: Cl 15.39, 15.40. $C_{11}H_9N_2SCl$. Calculated %: Cl 15.01.

2-Methyl-5-(β-cyano-β-chloroethyl)-benzothiazole (II). The base was obtained similarly to the 2-methyl-6-(β-cyano-β-chloroethyl)-benzothiazole, from diazotized 2-methyl-5-aminobenzothiazole and acrylonitrile. Nitrogen was evolved slowly. The mixture was stirred at room temperature for 5 hours. On the following day the mixture was heated in a water bath at 40° and stirred at this temperature for 1.5 hours. During the chromatographic purification of the base, chloroform was used as eluent. There was obtained a crystalline yellow mass, which was mixed with 25 ml boiling alcohol, and the residue was filtered and dried. Yield 12 g (50%). The base was crystallized from propanol. Yield 10.4 g (44%). Large lustrous plates, m.p. 159-161°. After a second crystallization from alcohol and the application of bone char, the melting point was unchanged.

Found %: Cl 15.31, 15.34. $C_{11}H_9N_2SCl$. Calculated %: Cl 15.01.

2-Methyl-6-β-cyanovinylbenzothiazole (III). A solution of 11.8 g (0.05 g-mole) 2-methyl-6-(β-cyano-β-chloroethyl)-benzothiazole in 60 ml dry quinoline was heated 1 hour at 185-190°. The quinoline was removed by steam distillation, and the residue in the flask (solid lumps) was pulverized, filtered off, washed with water, and dried. The substance did not contain halogen. The base was dissolved in benzene and the solution was twice chromatographed on aluminum oxide. There was obtained 8 g of white residue with m.p. 136-138°. Finally, the base was crystallized from 50% aqueous alcohol with the application of bone char. Long colorless needles, m.p. 137-138°. Yield 5.9 g (65%).

Found %: S 15.95, 16.16. $C_{11}H_8N_2S$. Calculated %: S 16.00.

Appearance of dye	Yield, %	Melting point	Empirical formula	Found		Calculated	
				element	content, %	element	content, %
Green crystals	35	289—292° (decomp.)	$C_{31}H_{30}O_3N_4S_3$	S	14.80, 14.59	S	15.04
The same	30	272—273 (decomp.)	$C_{35}H_{32}O_2N_4S_3$	N	8.58, 8.65	N	8.58
Dark-green crystals	27	267—268 (decomp.)	$C_{36}H_{31}O_3N_4S_3$	N	8.15, 8.04	N	8.40
The same	46	359—362 (decomp.)	$C_{31}H_{30}O_3N_4S_3$	S	14.79, 14.72	S	15.04
"	43	281—282 (decomp.)	$C_{35}H_{32}O_3N_4S_3$	N	8.34, 8.42	N	8.58
"	53	274—275 (decomp.)	$C_{36}H_{31}O_3N_4S_3$	N	8.68, 8.69	N	8.40
Green crystals	25	326—329	$C_{38}H_{31}O_3N_4S$	N	8.72	N	8.94
The same	22	238—239 (decomp.)	$C_{36}H_{32}O_3N_4S_3$	N	8.66, 8.76	N	8.37
"	18	282 (decomp.)	$C_{36}H_{32}O_3N_4S_3$	N	8.34, 8.33	N	8.37
Dark-green crystals	20	245 (decomp.)	$C_{39}H_{35}N_2S_2Br$	N	4.14, 4.35	N	4.14
The same	17	268—269	$C_{39}H_{35}N_2S_2Br$	N	4.62, 4.61	N	4.14
Crystals with bronze luster	51	287—288	$C_{19}H_{17}ON_3S_3$	S	24.82, 24.75	S	24.56
Red crystals	44	308—310	$C_{19}H_{17}ON_3S_3$	S	24.72, 24.87	S	24.56
Lustrous dark crystals	30	310—312	$C_{21}H_{19}ON_3S_2$	N	10.13, 10.10	N	10.68

2-Methyl-5-β-cyanovinylbenzothiazole (IV). 8.2 g (0.035 g-mole) 2-methyl-5-(β-cyano-β-chloroethyl)-benzothiazole and 45 ml quinoline were heated 2 hours at 185-190°. The residue obtained was dried, dissolved in chloroform, and chromatographed on aluminum oxide. The base was crystallized from benzene and then from alcohol. Yield 4.2 g (60%). Colorless crystals, m.p. 142-143°.

Found %: S 15.96, 15.98. $C_{11}H_8N_2S_2$. Calculated %: S 16.00.

6-β-Cyanovinylquinaldine (V). 15.8 g (0.1 g-mole) 6-aminoquinaldine was diazotized as indicated above. 100 ml acetone, 5.3 g (0.1 g-mole) acrylonitrile, 27.2 g sodium acetate, and 5.2 g cupric chloride in 12 ml water was introduced into the reactor. There was obtained 3 g of an oil, which solidified upon cooling. It was found that a mixture of chloro-derivative and 6-β-cyanovinylquinaldine had been obtained; therefore without further purification the mixture was subjected to heating in quinoline for 1.5 hours at 185-190°. After the dehydrochlorination and chromatography on aluminum oxide, there was obtained 1.2 g (48%) of the base, m.p. 133-136°. Then the substance was crystallized from methanol. Yield 0.6 g (24%). Colorless crystals, m.p. 140-141°.

Found %: N 14.30, 14.38. $C_{13}H_{10}N_2$. Calculated %: N 14.41.

Ethyl-p-toluenesulfonate of 2-Methyl-6-β-cyanovinylbenzothiazole. 2 g (0.01 g-mole) 2-methyl-6-β-cyanovinylbenzothiazole and 2.5 g (0.0125 g-mole) ethyl ester of p-toluenesulfonic acid were heated in a paraf-

fin bath at 145-150° (in the paraffin) for 6 hours. The quaternary salt was dissolved in hot water; the solution was washed with benzene, boiled with bone char, filtered, and evaporated on a steam bath. Yield 3.6 g (90%).

Ethyl-p-toluenesulfonate of 2-Methyl-5-β-cyanovinylbenzothiazole. 2 g 2-methyl-5-β-cyanovinylbenzothiazole and 2.5 g ethyl ester of p-toluenesulfonic acid were heated at 135-140° for 5 hours. Yield 3.7 g (92%).

Dyes

Thiacarbocyanines were obtained under standard conditions. 0.8 g (0.002 g-mole) ethyl-p-toluenesulfonate of 2-methyl-β-cyanovinylbenzothiazole, 0.8 g ester of orthocarboxylic acid, and 4 ml dry pyridine were boiled 12-15 minutes. At the end of the heating a thick paste of crystals precipitated. After cooling, the residue (dye) was filtered off, washed with water, a small quantity of methanol, and ether, and crystallized from a suitable solvent. The quinocarbocyanine was obtained similarly from 0.39 g ethyl-p-toluenesulfonate of 6-β-cyanovinylquinaldine and orthoformic ester.

Thiadicarbocyanines. 0.8 g (0.002 g-mole) ethyl-p-toluenesulfonate of 2-methyl-β-cyanovinylbenzothiazole (or correspondingly 0.9 g ethyl-p-toluenesulfonate of 2-methylstyrylbenzothiazole), 0.25 g (0.001 g-mole) dianilmalonic aldehyde hydrochloride, 4 ml dry pyridine, and 15 drops piperidine were boiled 15 minutes. In the case of the β-cyanovinyl derivatives, 10-15 ml alcohol was added to the reaction mixture. The precipitated residue (dye) was filtered off and crystallized from pyridine. For styryldicarbocyanines, 20-25 ml alcohol was added to the hot reaction mixture, and the dye was precipitated by the addition of hot aqueous solution of potassium bromide and crystallized from pyridine and then from alcohol.

Dimethinemerocyanines. 0.8 g (0.002 g-mole) ethyl-p-toluenesulfonate of 2-methyl-β-cyanovinylbenzothiazole was dissolved in 15 ml anhydrous alcohol. To the solution there was added 0.61 g (0.002 g-mole) 3-ethyl-5-acetanilidomethylene-rhodanine and 1 ml triethylamine, and the mixture was heated on a steam bath for 12-15 minutes. The precipitated residue of the merocyanine was filtered off, washed with water, methanol, and ether, and crystallized. Table 4 shows data on the synthesis of the carbocyanines, thiadicarbocyanines, and dimethinemerocyanines.

SUMMARY

1. By the interaction of benzothiazolyldiazonium chlorides with acrylonitrile, 2-methyl-5- and 2-methyl-6-(β-cyano-β-chloroethyl)-benzothiazoles were obtained; after dehydrochlorination these were converted to 2-methyl-5- and 2-methyl-6-β-cyanovinylbenzothiazoles.

2. From the bases, quaternary salts were obtained, and from the salts, cyanine dyes containing β-cyanovinyl radicals on the benzothiazole rings. Analogous bases and dyes were obtained from 6-aminoquinaldine.

3. It was shown that the absorption peaks of the thiacyanines obtained differ little from the absorption peaks of the corresponding thiacyanines containing styryl groups on the benzothiazole or quinoline ring.

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STUDIES IN THE FIELD OF THE CHEMISTRY OF CYANINE DYES

XV. CYANINE DYES CONTAINING PHTHALIMIDE GROUPS AS SUBSTITUENTS

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Cyanine dyes containing amine and acetylamine groups on the heterocyclic rings were described some time ago [1-5]; diacylamino derivatives up to now have been unknown. In the present work the synthesis of a number of phthalimino derivatives of thiacyanines is presented.

By analogy with the synthesis of phthalimide [6] or phenylphthalimide [7], phthalic anhydride was melted with aminobenzothiazoles, aminobenzoxazoles, and aminoquinolines. High-melting and well-crystallized phthalimides were obtained. A list of the new bases which we synthesized is given in Table 1.

Some of the listed bases were heated with the ethyl ester of p-toluenesulfonic acid to obtain the quaternary salts. The latter upon condensation with orthocarboxylic esters formed carbocyanines. Table 2 shows the absorption peaks (in mμ) of certain phthalimidocarbocyamines. The table also shows for comparison the absorption peaks of aminothiacarbocyanines [1-4].

From the data of Table 2 it is evident that amino groups on the 5,5'- or 6,6'-positions of the thiacarbocyanine give rise to a strong bathochromic effect, the magnitude of the effect being almost identical for the 6- and 5-amino substitution [4].

Acetylation of the amine group reduces the mobility of the electron pair at the nitrogen atom of the amino-group and thus weakens the bathochromic effect. Further acylation of the amino group with the aid of phthalic anhydride almost completely binds the electron pair of the amino group, as a result of which its influence on color almost disappears.

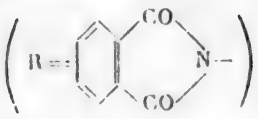
From the quaternary salts (containing phthalimide radicals) there were also prepared certain styryl dyes and monomethinethiacyanines, the absorption peaks of which are shown in Table 3.

The ethiodide of 2-(p-dimethylaminostyryl)-benzothiazole has an absorption peak at 530 mμ, and 3,3'-diethylmonomethinethiacyanine iodide at 422 mμ. Thus, the introduction of the phthalimide group into the molecule of monomethinecyanine or styryl dye causes a significant shift of the absorption peak to the long-wave region of the spectrum.

The initial primary amines of the nitrogen-containing heterocyclic bases were prepared by reduction of the corresponding nitro compounds. For some of them the directions for synthesis were defined more precisely. Vacuum distillation of the amines permitted significant increases of yields.

TABLE 1

Phthalimides



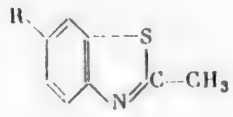
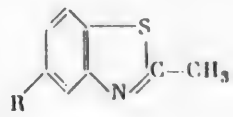
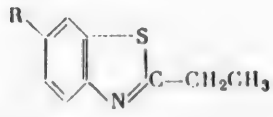
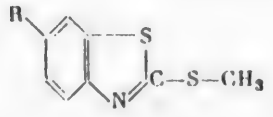
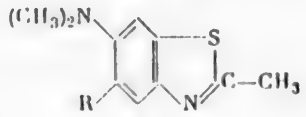
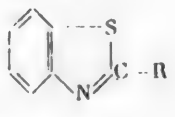
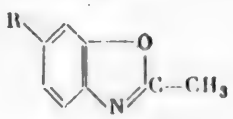
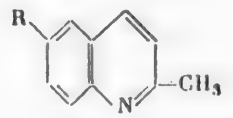
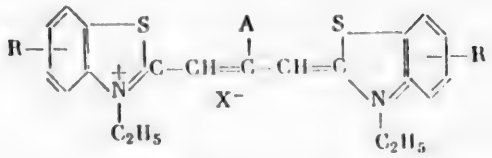
Compound No.	Phthalimido-derivative	Yield, %	Melting point
(I)		70	219°
(II)		82	247
(III)		77	157
(IV)		80	210
(V)		56	214—215
(VI)		75	247—248
(VII)		60	239—240
(VIII)		71	205—206

TABLE 2

Phthalimidothiacarbocyanines



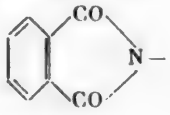
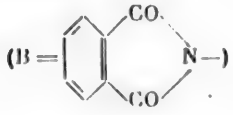
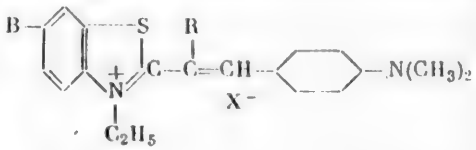
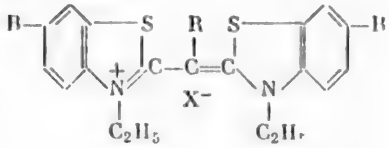
Compound No.	Significance of R	Position of substituent R	Absorption peak, mμ	
			A=H	$A=C_2H_5$
--	H	—	560	550
—	NH_2	6,6′	597	--
	$NHCOCH_3$	6,6′	581	--
—	NH_2	5,5′	596	—
—	$NHCOCH_3$	5,5′	577	—
(IX, X)		6,6′	568	558
(XI, XII)		5,5′	568	558

TABLE 3

Dyes



Compound No.	Formula	Significance of R	Absorption peak, mμ
(XIII)		H	538
(XIV)		CH_3	470
(XV)		H	445
(XVI)		CH_3	497

The synthesis of 2-methyl-6-aminobenzoxazole is given in the literature [8]. The authors of this work recommend that after reduction the hot mixture should be neutralized with sodium carbonate, after which the solution is evaporated under vacuum. As indicated by the authors, the yield constitutes 50%. We set up five experiments,

but in none of them did the yield of 2-methyl-6-aminobenzoxazole exceed 4-6%. In the residue there was a dark mass of a violet color. Probably the amine is readily oxidized in the alkaline medium; therefore, in subsequent work the separation of the product was conducted in acetic acid medium, whereupon the yield of the amine reached 45-50%.

6-Nitroquinaldine is described in the literature [9]. In order to moderate the reaction between paraldehyde and p-nitroaniline, we used methanol as a diluent.

EXPERIMENTAL

2-Ethyl-6-aminobenzothiazole. To a three-necked flask, equipped with stirrer, reflux condenser, and thermometer, there were introduced 20.8 g of 2-ethyl-6-nitrobenzothiazole [10] and 115 ml concentrated hydrochloric acid. The contents of the flask were heated in a water bath to 55-65°, and 19.2 g of spongy tin was added over 2.5-3 hours with stirring. Then the mixture was stirred for three hours at 65-70° and allowed to stand overnight. After adding 200 ml of water, the mixture was heated until the sediment was completely dissolved. The solution was filtered and cooled; then excess sodium hydroxide (first 15%, then 40%) was added with stirring until the tin salts were completely dissolved. The gray residue was filtered off, washed with cold water, dried, and vacuum distilled. Yield 16.1 g (90%). B.p. 182-183° at 2-3 mm, m.p. 72° (from toluene). Colorless large flakes.

Found %: N 15.90, 15.92. $C_9H_{10}N_2S$. Calculated %: N 15.73.

2-Ethyl-6-acetylaminobenzothiazole. Acetic anhydride (10 g) was added slowly to a solution of 10.6 g of 2-ethyl-6-aminobenzothiazole in 40 ml benzene. The mixture was heated 40 minutes on a steam bath, the benzene was completely distilled off, the residue was poured into water, and the precipitate was filtered off and crystallized from 50% aqueous alcohol. Yield 9.5 g (72%). Colorless prisms, m.p. 138°.

2-Methyl-6-aminobenzothiazole. 58.2 g of 2-methyl-6-nitrobenzothiazole (m.p. 163-164°) was reduced by 59 g of spongy tin in 310 ml hydrochloric acid. The sediment was dissolved in 250 ml water, filtered, cooled, and neutralized (with stirring) with sodium hydroxide solution. About 350 ml of 40% sodium hydroxide solution was required for neutralization and dissolving the tin salts. Yield of amine 47.2 g (95%). B.p. 169-171° at 2-3 mm; m.p. 118-119°.

2-Methyl-5-aminobenzothiazole was obtained by a method which we had developed previously [11].

2-Methyl-5-acetylaminobenzothiazole was obtained from 16.4 g of the amine and 13 g acetic anhydride in 50 ml benzene. After crystallization from a mixture of 65 ml alcohol and 20 ml water, yield 19 g (91%). Colorless lustrous flakes, m.p. 160-161° (m.p. 157° [12]).

2-Methylmercapto-6-aminobenzothiazole. 22.6 g of 2-methylmercapto-6-nitrobenzothiazole [13] and 115 ml concentrated hydrochloric acid were heated in a water bath to 65-70°. There was added to the mixture with stirring (caution; severe foaming!) a solution of 45 g stannous chloride in 57 ml concentrated hydrochloric acid. The mass was heated on a steam bath for 1 hour, after which another batch of 45 g stannous chloride in 57 ml concentrated hydrochloric acid was added, and heating was continued for 30 minutes. The mixture was diluted with 300 ml water, heated until all sediment was dissolved, and after cooling was treated with 40% sodium hydroxide solution. The amine was dissolved in methanol, filtered, the solvent was distilled off, and the residue was vacuum distilled. Yield 15.7 g (80%). B.p. 185-187° at 2-3 mm, m.p. 109-100°. It was necessary to conduct the distillation at 2-3 mm; at higher pressures the amine begins to decompose severely.

The acetyl derivative was obtained as indicated above. After crystallization from alcohol, yield 75%, m.p. 167°.

2-Methyl-6-aminobenzoxazole. 28.2 g of 2-methyl-6-nitrobenzoxazole [8] was added in small portions to a boiling mixture consisting of 34 g cast-iron filings, 90 ml water, and 15 ml glacial acetic acid. After adding all of the nitro product, the mixture was boiled for 1.5 hours and then filtered. The sediment was washed on the filter with 150 ml of hot water. The aqueous solution was evaporated on a steam bath. After drying at 100° the residue was extracted three times with boiling benzene (150 ml). The solution was filtered, and the benzene was boiled off to a volume of 40 ml. Upon cooling the solution, the amine precipitated. Yield 12.4 g (53%), m.p. 138-140°. After recrystallizing from benzene, m.p. 146-147°.

TABLE 4

Compound No.	Name	Quantity of reactants, g: amine	Quantity of reactants, g: phthalic anhydride	Solvent for crystallization	Empirical formula	% N: found	% N: calculated
(I)	2-Methyl-6-phthalimidobenzothiazole	4.9	4.4	Butyl alcohol	$C_{16}H_{10}O_2N_2S$	9.50, 9.61	9.52
(II)	2-Methyl-5-phthalimidobenzothiazole	3.2	2.9	Isoamyl alcohol	$C_{16}H_{10}O_2N_2S$	9.47, 9.57	9.52
(III)	2-Ethyl-6-phthalimidobenzothiazole	3.5	2.9	Butyl alcohol	$C_{17}H_{12}O_2N_2S$	9.07, 8.97	9.09
(IV)	2-Methylmercapto-6-phthalimidobenzothiazole	3.8	2.9	Isoamyl alcohol	$C_{16}H_{10}O_2N_2S_2$	8.69, 8.76	8.59
(V)	2-Methyl-6-dimethylamino-5-phthalimidobenzothiazole	4.1	2.9	Butyl alcohol	$C_{18}H_{15}O_2N_3S$	12.32, 12.60	12.45
(VI)	2-Phthalimidobenzothiazole	3	2.9		$C_{15}H_8O_2N_2S$	10.07, 10.18	10.00
(VII)	2-Methyl-6-phthalimidobenzoazole	2.9	2.9		$C_{16}H_{10}O_3N_2$	9.96, 9.84	10.07
(VIII)	2-Methyl-6-phthalimidoquinoline	3.1	2.9		$C_{24}H_{12}O_2N_2$	9.98, 10.11	9.72

6-Nitroquinaldine. Into a two-liter flask there were introduced (in order) 70 g of p-nitroaniline, 750 ml methanol, 500 ml water, 80 ml paraldehyde, and 60 ml concentrated hydrochloric acid. The mixture was refluxed on a steam bath for 3 hours, diluted with 1400 ml water, and allowed to stand until the following day. The liquid was decanted from the reddish-brown oil and neutralized (cooling to 11-12°) with 150 ml of 20% sodium hydroxide solution. The yellowish-green precipitate was filtered off, washed with water, dried at 60°, and crystallized from 1300 ml of methanol. Weight 57 g, m.p. 164-165°. The mother liquor was reduced in volume by distillation of 900 ml of the methanol. Upon cooling an additional 11 g of the nitro product precipitated, with m.p. 159-160°. Total weight 68 g. Finally, the product was crystallized from 1050 ml alcohol, using bone char (hot filtration). Yield 52 g (27%). M.p. 172-173° (m.p. 164° [9], 165° [14]).

6-Aminoquinaldine. 56.7 g of 6-nitroquinaldine and 360 ml concentrated hydrochloric acid were placed in a three-necked flask. The mixture was heated with stirring to 60° in a water bath until all of the nitroquinaldine was dissolved; then 72 g of spongy tin was added in small portions over 1.5 hours, so that the mixture temperature did not exceed 70°. Then the material was stirred 3 hours at 65-70° and allowed to stand overnight. The sediment was filtered off, pressed on the filter, dissolved in 900 ml hot water, and filtered. The solution after cooling was neutralized with 1500 ml of 30% sodium hydroxide solution. The amine was filtered off, washed with cold water, and dried. Weight 43.7 g (92%), m.p. 186-187°. The product was crystallized from aqueous alcohol (300 ml alcohol and 600 ml water). Yield 36.2 g (76%). M.p. 190-191° (m.p. 187-188°) [9].

General Method of Synthesis of Phthalimides. Molar quantities of the amine and phthalic anhydride were heated to 185-140°. At this temperature, vigorous evolution of water vapor and solidification of the melt were observed. Then the temperature was increased until the product remelted (215-230°) and the mixture was held at this temperature for 3-5 minutes until the evolution of water vapor had completely ceased. The still-liquid mass was poured into a mortar, pulverized, and washed with boiling alcohol; the phthalimide product was subjected to crystallization. For analysis, the preparations were recrystallized from alcohol. Table 4 shows the conditions of synthesis of the phthalimides and the results of analysis.

Ethyl-p-toluenesulfonate of 2-Methyl-6-phthalimidobenzothiazole. 2.9 g of 2-methyl-6-phthalimidobenzothiazole and 6 g of the ethyl ester of p-toluenesulfonic acid were heated in an oil bath at 150-160° for 7 hours. The contents of the flask were dissolved in boiling water, the aqueous solution was washed with benzene,

boiled with bone char, and evaporated on a steam bath; finally, the salt was heated to 120-125° (with vigorous stirring with a thermometer immersed in the material). Yield 4.7 g (95%).

Ethyl p-toluenesulfonate of 2-Methyl-5-phthalimidobenzothiazole was prepared similarly from 2.9 g 2-methyl-5-phthalimidobenzothiazole and 6 g of the ethyl ester of p-toluenesulfonic acid. Yield 4.5 g (91%).

Ethyl p-toluenesulfonate of 2-Ethyl-6-phthalimidobenzothiazole. 3 g of 2-ethyl-6-phthalimidobenzothiazole and 6 g of the ethyl ester of p-toluenesulfonic acid were heated 10 hours at 160-165°. Yield of quaternary salt 4.2 g (82%).

Ethyl p-toluenesulfonate of 2-Methylmercapto-6-phthalimidobenzothiazole. 3.2 g of the base and 6 g of the ethyl ester of p-toluenesulfonic acid were heated 12 hours at 150-160°. Yield 3.9 g (75%).

Dyes

3,3'-Diethyl-6,6'-diphthalimidothiacarbocyanine Iodide (IX). A mixture of 0.98 g of the ethyl p-toluenesulfonate of 2-methyl-6-phthalimidobenzothiazole, 1 g of orthoformic ester, and 6 ml acetic anhydride was boiled for 15 minutes, then poured into a hot aqueous solution of potassium iodide. The precipitate was filtered off and crystallized from alcohol. Fine crystals with bronze luster, m.p. 220-223°. Yield 0.23 g (29%).

Found %: N 6.93, 6.74. $C_{37}H_{27}O_4N_4S_2I$. Calculated %: N 7.16.

3,3',9-Triethyl-6,6'-diphthalimidothiacarbocyanine Iodide (X). 0.98 g of the quaternary salt, 1 g of orthopropionic ester, and 5 ml of acetic anhydride were boiled for 25 minutes. The dye was precipitated by water. The viscous mass was separated and dissolved in methanol, and the dye was precipitated by potassium iodide and crystallized from alcohol. Fine, dark-colored crystals, m.p. 215-216°. Yield 0.18 g (24%).

Found %: N 7.29, 7.23. $C_{39}H_{31}O_4N_4S_2I$. Calculated %: N 6.91.

3,3'-Diethyl-5,5'-diphthalimidothiacarbocyanine Iodide (XI) was obtained similarly from 0.98 g of the ethyl p-toluenesulfonate of 2-methyl-5-phthalimidobenzothiazole, 1 g of orthoformic ester, and 7 ml of acetic anhydride. Fine crystals with bronze luster, m.p. 229-230°. Yield 0.25 g (34%).

Found %: N 7.09, 6.96. $C_{37}H_{27}O_4N_4S_2I$. Calculated %: N 7.16.

3,3',9-Triethyl-5,5'-diphthalimidothiacarbocyanine Iodide (XII) was prepared similarly to the dye (X). Fine black crystals, m.p. 212-214°. Yield 0.16 g (21%).

Found %: N 7.29, 7.35. $C_{39}H_{31}O_4N_4S_2I$. Calculated %: N 6.91.

Ethiodide of 2-(p-dimethylaminostyryl)-6-phthalimidobenzothiazole (XIII). A mixture of 0.49 g of the ethyl p-toluenesulfonate of 2-methyl-6-phthalimidobenzothiazole, 0.15 g of p-dimethylaminobenzaldehyde, and 5 ml acetic anhydride was boiled for 30 minutes. The dye was precipitated by aqueous potassium iodide solution and crystallized from alcohol. Crystals of a dark-cherry color, m.p. 231-233° (decomp.).

Found %: N 7.42, 7.52. $C_{27}H_{24}O_2N_3SI$. Calculated %: N 7.22.

Ethiodide of 2-(p-Dimethylamino-β-methylstyryl)-6-phthalimidobenzothiazole (XIV) was prepared under analogous conditions from 0.5 g of the ethyl p-toluenesulfonate of 2-ethyl-6-phthalimidobenzothiazole and 0.15 g of p-dimethylaminobenzaldehyde. Dark-red crystals, m.p. 205-206° (decomp.). Yield 0.14 g (23%).

Found %: N 7.01, 6.85. $C_{28}H_{26}O_2N_3SI$. Calculated %: N 7.05

SUMMARY

1. By melting aminobenzothiazoles, aminobenzoxazoles, and aminoquinolines with phthalic anhydride, the corresponding phthalimido derivatives have been obtained.

2. The benzothiazolylphthalimides were converted to quaternary salts, and the latter to cyanine dyes containing phthalimide radicals on the benzothiazole ring.

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STUDIES IN THE FIELD OF THE CHEMISTRY OF CYANINE DYES

XVI. BIS-CYANINES

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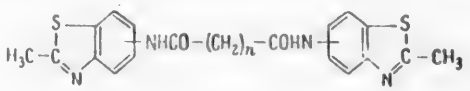
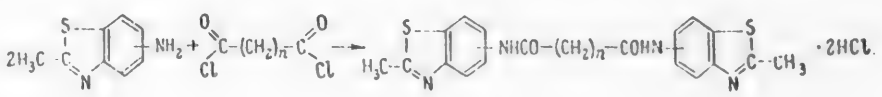
A. I. Kiprianov and I. K. Ushenko [1] in 1940 synthesized cyanine dyes in which the molecules were coupled through the nitrogen atoms by unsaturated chains. These were called "bis-cyanines" by analogy with bis-azo dyes. Considerably later Brooker and Sprague described in patents [2-4] the synthesis of analogous bis-cyanines. Brooker [2] noted that the bis-cyanines which they synthesized are low-solubility and nondispersing dyes, which are suitable mainly for sensitizing color film. In numerous patents, Wilson and the firm Gevaert [5, 6] also listed cyanines coupled by unsaturated hydrocarbon chains. Among the bis-cyanines are the bis-thiazolocyanines described by Hensley [7] and E. D. Sych [8], and also bis-cyanines with disconnected chromophores, synthesized by Schwarz [9].

The present communication describes bis-cyanines obtained from 2,2'-dimethyldibenzothiazolylurea:

and also from the analogous substituted diamides of dicarboxylic acids, where n = 1, 2, 3,4.



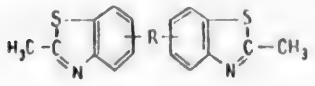
The starting materials for the synthesis of the indicated bases were 2-methyl-6-amino- and 2-methyl-5-aminobenzothiazole, which, upon interaction with phosgene or with dibasic acid chlorides in benzene solution, form diamides.



All of these substituted diamides are poorly soluble in [ethyl] alcohol, and by comparison readily soluble in boiling butyl or isoamyl alcohol.

TABLE 1

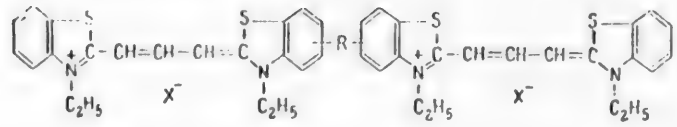
Di-(2-methylbenzothiazolyl)-diamides



Compound No.	R	Position of substituent R	Yield, %	Melting point
I	—NH—CO—HN—	6, 6′	42	281°
II	—NH—CO—CO—HN—	6, 6′	56	279
III	—NH—CO—CH_2—CO—HN—	6, 6′	37	232
IV	—NH—CO—$(CH_2)_2$—CO—HN—	6, 6′	72	260
V	—NH—CO—$(CH_2)_3$—CO—HN—	6, 6′	46	210
VI	—NH—CO—$(CH_2)_4$—CO—HN—	6, 6′	41	247
VII	—NH—CO—HN—	5, 5′	44	263
VIII	—NH—CO—CO—HN—	5, 5′	69	343
IX	—NH—CO—CH_2—CO—HN—	5, 5′	33	270
X	—NH—CO—$(CH_2)_2$—CO—HN—	5, 5′	60	257
XI	—NH—CO—$(CH_2)_3$—CO—HN—	5, 5′	44	227
XII	—NH—CO—$(CH_2)_4$—CO—HN—	5, 5′	65	248

TABLE 2

Bis-thiacarbocyanines



Compound No.	R	Position of substituent R	Absorption peak, mμ	Displacement of absorption peak, mμ
XIII	—NH—CO—HN—	6, 6′	568	+10
XIV	—NH—CO—CO—HN—	6, 6′	565	+ 7
XV	—NH—CO—CH_2—CO—HN—	6, 6′	571	+13
XVI	—NH—CO—$(CH_2)_2$—CO—HN—	6, 6′	566	+ 8
XVII	—NH—CO—$(CH_2)_3$—CO—HN—	6, 6′	570	+12
XVIII	—NH—CO—$(CH_2)_4$—CO—HN—	6, 6′	571	+13
XIX	—NH—CO—HN—	5, 5′	567	+ 9
XX	—NH—CO—CO—HN—	5, 5′	565	+ 7
XXI	—NH—CO—CH_2—CO—HN—	5, 5′	570	+12
XXII	—NH—CO—$(CH_2)_2$—CO—HN—	5, 5′	565	+ 7
XXIII	—NH—CO—$(CH_2)_3$—CO—HN—	5, 5′	568	+10
XXIV	—NH—CO—$(CH_2)_4$—CO—HN—	5, 5′	570	+12

The new diamides with an even number of methylene groups are higher-melting than those with odd numbers (this is analogous to the corresponding dicarboxylic acids). The symmetrical di-(2-methylbenzothiazolyl)-diamides upon heating with the ethyl ester of p-toluenesulfonic acid readily form diquaternary salts. The yields and melting points of the new bases are shown in Table 1.

Twelve diquaternary salts were prepared under the usual conditions from the new bases and the ethyl ester of p-toluenesulfonic acid. These salts were condensed with the ethiodide of 2-acetanilidovinylbenzothiazole in

TABLE 3

Compound No.	Name	Initial amine	Quantity of dibasic acid chloride, g	Solvent for crystallization, ml	Yield, g	Empirical formula	% N found	% N calc.
II	Di-N,N'-[2-methylbenzothiazolyl-(6)]-oxamide	2-Methyl-6-aminobenzothiazole	Oxalyl chloride (0.8)	Isoamyl alcohol (800)	1.3	$C_{18}H_{14}O_2N_4S_2$	14.36, 14.47	14.65
III	Di-N,N'-[2-methylbenzothiazolyl-(6)]-malonamide	The same	Malonyl chloride (1)	Butyl alcohol (70)	1.2	$C_{19}H_{16}O_2N_4S_2$	13.61	14.14
IV	Di-N,N'-[2-methylbenzothiazolyl(6)]-succinamide	» »	Succinyl chloride (0.94)	Propyl alcohol (60)	1.8	$C_{20}H_{18}O_2N_4S_2$	13.60, 13.41	13.65
V	Di-N,N'-[2-methylbenzothiazolyl-(6)]-glutaramide	» »	Glutaryl chloride (1)	Methyl alcohol (75)	1.2	$C_{21}H_{20}O_2N_4S_2$	13.00	13.20
VI	Fi-N,N'-[2-methylbenzothiazolyl-(6)]-adipamide	» »	Adipyl chloride (1.1)	Propyl alcohol (60)	1.1	$C_{22}H_{22}O_2N_4S_4$	12.61, 12.54	12.78
VIII	Di-N,N'-[2-methylbenzothiazolyl-(5)]-oxamide	2-Methyl-5-aminobenzothiazole	Oxalyl chloride (0.8)	Acetophenone (120)	1.6	$C_{18}H_{14}O_2N_4S_4$	14.40, 14.31	14.65
IX	Di-N,N'-[2-methylbenzothiazolyl-(5)]-malonamide	The same	Malonyl chloride (1)	Butyl alcohol (55)	0.8	$C_{19}H_{16}O_2N_4S_4$	13.63	14.14
X	Di-N,N'-[2-methylbenzothiazolyl-(5)]-succinamide	» »	Succinyl chloride (0.94)	Butyl alcohol (40)	1.5	$C_{20}H_{18}O_2N_4S_4$	13.57, 13.48	13.65
XI	Di-N,N'-[2-methylbenzothiazolyl-(5)]-glutaramide	» »	Glutaryl chloride (1)	Ethyl alcohol (75)	1.15	$C_{21}H_{20}O_2N_4S_4$	13.09, 12.90	13.20
XII	Di-N,N'-[2-methylbenzothiazolyl-(5)]-adipamide	» »	Adipyl chloride (1.1)	Butyl alcohol (70)	1.7	$C_{22}H_{22}O_2N_4S_4$	12.68, 12.58	12.78

pyridine medium. This reaction gave bis-thiacarbocyanines, the absorption peaks of which are shown in Table 2. 3,3-Diethylthiacarbocyanine iodide has an absorption peak at 558 mμ.

From the data presented in Table 2 it follows that coupling two molecules of the thiacarbocyanine on the 6,6'- or 5,5'-positions through diamide groups gives rise to a 7-13 mμ shift of the absorption peak of the bis-cyanine toward the long-wave region of the spectrum.

The bis-thiacarbocyanines which we synthesized have high molecular weights. All of them upon recrystallization are precipitated in the form of fine crystals which are difficult to purify completely. In view of these circumstances, some of the bis-thiacarbocyanines were not successfully isolated in analytically pure form.

EXPERIMENTAL

Malonyl chloride [10], oxalyl chloride [11], 2-methyl-5-aminobenzothiazole [12], and 2-methyl-6-aminobenzothiazole [13] were prepared in accordance with the literature.

General Method of Synthesis of 2,2'-Dimethyldibenzothiazolylamides. 2 g of 2-methyl-5-amino- or 2-methyl-6-aminobenzothiazole was dissolved in 40-50 ml of dry benzene and the calculated quantity of the particular dibasic acid chloride (dissolved in 5 ml of benzene) was added. The mixture was heated on a steam bath for 3 hours. After cooling, the precipitate was filtered off, washed with hot benzene, dried, heated to 60-70° with 10% sodium hydroxide, again filtered off, washed with warm water, dried, and subjected to crystallization. The 2,2'-dimethyldibenzothiazolylamides which we obtained are listed in Table 3.

Di-N,N'-[2-methylbenzothiazolyl-(6)]-urea (I). 2 g of 2-methyl-6-aminobenzothiazole was dissolved in 50 ml of benzene and phosgene was passed through the solution with stirring for 10 minutes. After standing for one day, the precipitate was filtered off and treated as indicated in the general method. After crystallization from 100 ml of butyl alcohol, yield 0.9 g (42%). White silky needles, m.p. 280-281°.

Found %: N 15.62, 15.57. $C_{17}H_{14}ON_4S_2$. Calculated %: N 15.81.

Di-N,N'-[2-methylbenzothiazolyl-(5)]-urea (VII) was obtained similarly [to the preparation of (I)] from 2 g of 2-methyl-5-aminobenzothiazole. After crystallization from 120 ml of isoamyl alcohol, yield 0.95 g (44.8%). Colorless flakes, m.p. 263°.

Found %: N 15.50, 15.27. $C_{17}H_{14}ON_4S_2$. Calculated %: N 15.81.

Di-(ethyl-p-toluenesulfonates) of 2,2-Dimethylbenzothiazolylamides were obtained by heating the base (0.001 mole) and the ethyl ester of p-toluenesulfonic acid (0.005 mole) in an oil bath at 145-150° (oil bath temperature) for 12 hours. The salt was treated with boiling water, and the solution was washed with benzene, boiled with bone char, filtered, and evaporated on a steam bath. Finally, the salt was heated to 120-125° while stirring vigorously with a thermometer. The yields of diquaternary salts reached 80-90%.

Diethiodide of Di-N,N'-[2-methylbenzothiazolyl-(5)]-adipamide. 1.6 g of di-2-methylbenzothiazolyl-5-adipamide and 2.19 g of the ethyl ester of p-toluenesulfonic acid were heated at 145-150° for 12 hours. Yield 2.44 g (81%). 0.7 g of the di-(ethyl-p-toluenesulfonate) was dissolved in 5 ml of hot water, and the diethiodide was precipitated by the action of potassium iodide. After crystallization from water, m.p. 256°.

Found %: I 33.55, 33.77. $C_{26}H_{32}O_2N_4S_2I_2$. Calculated %: I 33.86.

Dyes

Bis-thiacarbocyanines were obtained under standard conditions. A mixture of the di-(ethyl-p-toluenesulfonate) of the di-(2-methylbenzothiazolyl)-amide, the ethiodide of 2-acetanilidovinylbenzothiazole, and 8-12 ml of pyridine was boiled 10-15 minutes. The dye was precipitated by the addition of hot aqueous potassium iodide solution. The precipitated dye was filtered off, washed several times with water, 2-3 ml of alcohol, and ether, and twice recrystallized from alcohol. Yields and analytical results for the bis-thiacarbocyanines are presented in Table 4. All of the bis-thiacarbocyanines melted with decomposition.

TABLE 4

Compound No.	Quantity of corresponding di(ethyl-p-toluenesulfonate), g	Quantity of ethiodide of 2-acetanilidovinylbenzothiazole, g	Yield, %	Melting point	Empirical formula	% I	
						found	calculated
XIII	0.4	0.48	40	242°	$C_{43}H_{42}ON_6S_4I_2$	25.00	24.19
XIV	0.5	0.57	47	239	$C_{44}H_{42}O_2N_6S_4I_2$	23.72 24.03	23.78
XV	0.5	0.57	44	211	$C_{45}H_{44}O_2N_6S_4I_2$	24.30	23.47
XVI	0.5	0.55	35	232	$C_{46}H_{46}O_2N_6S_4I_2$	24.10	23.17
XVIII	0.5	0.53	43	153	$C_{48}H_{50}O_2N_6S_4I_2$	23.03 23.03	22.59
XX	0.5	0.57	32	272	$C_{44}H_{42}O_2N_6S_4I_2$	23.88 24.20	23.78
XXI	0.5	0.57	34	194	$C_{45}H_{44}O_2N_6S_4I_2$	24.13	23.47
XXIII	0.5	0.54	44	164	$C_{47}H_{48}O_2N_6S_4I_2$	23.95	22.88

SUMMARY

1. By the action of phosgene and various dibasic acid chlorides on 2-methyl-6-amino- and 2-methyl-5-aminobenzothiazole in benzene solution, twelve new symmetrical di-(2-methylbenzothiazolyl)-diamides have been prepared. From these, the corresponding diquaternary salts have been prepared.

2. As a result of the condensation of the di-(ethyl-p-toluenesulfonates) of di-(2-methylbenzothiazolyl)-amides with the ethiodide of 2-acetanilidovinylbenzothiazole, there were obtained bis-thiacarbocyanines in which two simple thiacarbocyanine groups are connected in the 6,6'- and 5,5'-positions through a dicarboxylic acid diamide group.

3. It was established that the coupling of two simple thiacarbocyanine groups through the diamide radical gives rise to a slight bathochromic effect.

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SYNTHESIS OF CERTAIN 2,3-SUBSTITUTED DERIVATIVES OF 1,4-NAPHTHOQUINONE

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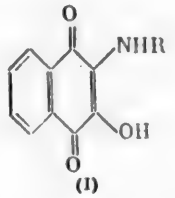
In earlier work [1] a description was given of a polarographic study of a large group of derivatives of 1,4-naphthoquinone with substituents in the 2,3-positions. Among the compounds studied, a considerable number were obtained for the first time. Data on the synthesis and properties of these new compounds are set forth in the present communication.

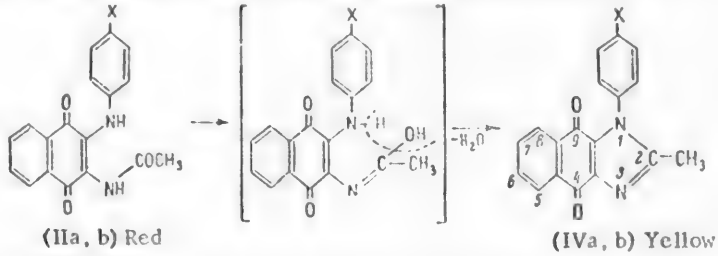
Derivatives of 2-amino-3-hydroxyl-1,4-naphthoquinone (I) are obtained by refluxing the 2,3-oxide of naphthoquinone with substituted amines in alcohol or acetic acid medium [2]. In such reactions it was possible only in the case of the sulfonamide derivatives [I, R = $C_6H_4SO_2NH_2$-(4)] to observe successfully the formation of the intermediate product – a light-colored dihydro compound. It is readily oxidized by atmospheric oxygen to the dark-colored quinone upon further boiling of the reaction mixture or upon recrystallization of the substance. The [required] duration of the reaction and the yields of hydroxyaminonaphthoquinones depend on the reactivity of the amine; with o-nitroaniline the reaction does not proceed at all, probably because of steric hindrance.



(I)

The hydroxyaminonaphthoquinones which were obtained (Table, Compounds 1-9) have deep colors—from blue to dark violet (blue-black), with various shades. Compounds of this group are difficultly soluble in the usual solvents; however, owing to the presence of the hydroxyl group, they are soluble in alkalies.

For obtaining derivatives of aminoacetaminonaphthoquinone (IIa, b), use was made of the behavior of 2-acetamino-3-chloronaphthoquinone in replacing the chlorine atom by various amines [3]. The resulting red products are converted to yellow naphthoquinoneimidazole derivatives (IVa, b), as it turned out, even upon prolonged refluxing in a high-boiling solvent.* This may be represented schematically as:



(IIa, b) Red
X = SO_2NH_2, COOH

(IVa, b) Yellow

* According to Fries [4], cyclization takes place upon boiling the analogous aniline derivative in alcoholic caustic solution or upon heating it to the melting point.

Properties of Derivatives of 2-Amino-3-Hydroxyl-1,4-naphthoquinone[a]

Prep. No.	Substituents in formula of 1,4-naphthoquinone	Reaction time, hr	Yield, %	Melting point	Appearance	Empirical formula	% N found	% N calculated
1	2-o-Chlorophenylamino-3-hydroxy-	9	25	189°	Reddish-violet needles	$C_{16}H_{10}O_3NCl$	4.78	4.66
2	2-p-Chlorophenylamino-3-hydroxy-	6	40	260	Violet plates	$C_{16}H_{10}O_3NCl$	4.88	4.66
3	2-(2,4-Dichlorophenylamino)-3-hydroxy-	24	40	241–242	Dark-violet with brown tinge	$C_{16}H_9O_3NCl_2$	4.19	4.17
4	2-p-Methoxyphenylamino-3-hydroxy-	4	45	194	Dark-violet plates	$C_{17}H_{13}O_4N$	4.83	4.74[b]
5	2-o-Methoxyphenylamino-3-hydroxy-	2	45	186–187	Dark-violet crystals	$C_{17}H_{13}O_4N$	4.82	4.74[c]
6	2-p-Sulfonamidophenylamino-3-hydroxy-	8	40	306	Blue crystals	$C_{16}H_{12}O_5N_2S$	7.76	8.16
7	2-p-Carboxyphenylamino-3-hydroxy-	3	63	306 (effervesces)	Violet needles (fibers)	$C_{17}H_{11}O_5N$	4.67	4.53[d]
8	2-p-Nitrophenylamino-3-hydroxy-	30	5	> 320 (does not melt)	Claret plates	$C_{16}H_{10}O_5N_2$	9.23	9.00[e]
9	2-m-Nitrophenylamino-3-hydroxy-	20	5	293–294	Brownish-claret	$C_{16}H_{10}O_5N_2$	10.17	9.0

[a]Difficultly soluble in alcohol, glacial acetic acid, benzene, acetone.
[b]Found %: OCH_3 10.37. Calculated %: OCH_3 10.51.
[c]Found %: OCH_3 10.46. Calculated %: OCH_3 10.51.
[d]Found %: C 65.78; H 3.64. Calculated %: C 66.02; H 3.56.
[e]Found %: C 61.85; H 3.29. Calculated %: C 61.93; H 3.23.

In addition, in this work there was carried out the reductive acetylation of certain derivatives of 1,4-naphthoquinone.

EXPERIMENTAL

2-(2,4-Dichlorophenyl)-amino-1,4-naphthoquinone. To a boiling solution of 1.75 g (0.01 g-mole) of 2-hydroxynaphthoquinone in 15 ml of ethanol there was added 1.64 g (0.01 g-mole) of 2,4-dichloroaniline. After 38-hour refluxing of the reaction mixture, the precipitate was filtered off and washed with alcohol. Weight 0.7 g (21%). From glacial acetic acid, orange needles with m.p. 203°. The substance is difficultly soluble in alcohol, readily soluble in glacial acetic acid.

Found %: N 4.40. $C_{16}H_9O_2NCl_2$. Calculated %: N 4.40.

2-p-Sulfonamidophenylamino-3-hydroxyl-1,4-naphthoquinone. 1.74 g (0.01 g-mole) of naphthoquinone oxide and 1.72 g of sulfanilamide, after 1 hour refluxing in alcohol solution, gave 0.75 g of blue precipitate with m.p. 302°. Upon further refluxing of the mother liquor, a whitish residue of the dihydro compound was precipitated (1 g in 8 hours); this upon refluxing in glacial acetic acid was converted to the quinone. Yield about 40%, m.p. 306°. Blue crystalline substance, very difficultly soluble in alcohol, glacial acetic acid, benzene, or acetone. Readily soluble in sodium hydroxide solution.

In an analogous manner, there were prepared derivatives of naphthoquinone with o- and p-chloroaniline, dichloroaniline, o- and p-anisidine, p-aminobenzoic acid, and m- and p-nitroaniline. Data on these substances are shown in the table.

2-p-Sulfonamidophenylamino-3-acetamino-1,4-naphthoquinone. To a boiling solution of 1 g acetaminochloronaphthoquinone in 20 ml butyl alcohol there was added 0.60 g of diethylaniline and 0.65 g of sulfanilamide. The solution gradually darkened, becoming dark-red, and a violet-red residue was precipitated. After 5 hour refluxing of the reaction mixture, the precipitate was filtered off and washed with hot alcohol. Weight 0.8 g (53%), m.p. 272° (from glacial acetic acid; red scales). Very difficultly soluble in alcohol, benzene, acetone, or glacial acetic acid. Rather difficultly soluble in nitrobenzene (0.1 g in 6 ml nitrobenzene). This sulfanilamide derivative melted at 272° if the capillary containing the substance was placed in a metallic block which had been preheated to this temperature. Upon prolonged gradual heating, the substance above 270° turned from red to yellow and did not melt upon further heating even at 340°.

Found %: N 10.65. $C_{18}H_{15}O_5N_3S$. Calculated %: N 10.90.

1-p-Sulfonamidophenyl-2-methyl-naphthimidazole-4,9-quinone (IVa). Obtained by heating the above-described compound at 230-260° for 20-30 minutes. The red crystalline substance was thereby converted to a yellow product (quantitative yield). From nitrobenzene, a yellow fine-crystalline powder (elongated rhombic), not melting even at 340°, insoluble in the usual solvents, difficultly soluble in nitrobenzene.

Found %: N 11.25. $C_{18}H_{13}O_4N_3S$. Calculated %: N 11.44.

2-p-Carboxyphenylamino-3-acetamino-1,4-naphthoquinone (IIb). 1.3 g (0.005 g-mole) of acetaminochloronaphthoquinone and 0.7 g of diethylaniline in 50 ml of alcohol was refluxed with 0.7 g of p-aminobenzoic acid. After cooling the solution, a red precipitate was filtered off; this after boiling twice with 20 ml of alcohol had a dark-raspberry color (plates). After two recrystallizations from alcohol (from 100 ml) there remained 0.3 g (20%) of the dark-raspberry product. The substance shriveled and grew lighter at 200°, but did not melt.

Found %: N 7.11; C 63.63; H 5.05. $C_{19}H_{14}O_5N_2 \cdot C_2H_5OH$. Calculated %: N 7.07; C 63.30; H 4.90. $C_{19}H_{14}O_5N_2$. Calculated %: N 8.0.

After drying over boiling xylene to constant weight, found, %: N 8.47. Apparently the substance upon drying loses, besides a molecule of alcohol, a molecule of water, and is partially cyclized. For the cyclized product, %: N 8.44.

1-p-Carboxyphenyl-2-methylnaphthimidazole-4,9-quinone (IVb). Obtained by carrying out the condensation of acetaminochloronaphthoquinone with p-aminobenzoic acid in butyl alcohol with prolonged refluxing of the reaction mixture (in [ethyl] alcohol the reaction proceeds very slowly and with low yield). The fine crystalline light-yellow precipitate was filtered from the hot solution. Difficultly soluble in alcohol. Yield low. M.p. 317° (from glacial acetic acid).*

Found %: N 8.65. $C_{19}H_{12}O_4N_2$. Calculated %: N 8.44.

2-Ethylphenylamino-3-acetamino-1,4-naphthoquinone. 0.65 g (0.0025 g-mole) of acetaminochloronaphthoquinone in 25 ml of alcohol was refluxed with 0.3 g of diethylaniline and 0.28 g of ethylaniline for 50 hours. The solution gradually acquired a violet color with a reddish tinge. The precipitate (formed upon cooling) was a mixture of brownish-red plates and yellow plates (initial material). Weight 0.32 g. After several recrystallizations from alcohol, the precipitate still was not homogeneous (0.18 g), m.p. 162°. The yield of 2-ethylphenylamino-acetamino-naphthoquinone was very low. The substance was very readily soluble in alcohol, acetone, benzene, or ether, giving a violet color. For purification it was necessary to evaporate a solution and to pick out (under a magnifying glass) the violet-red needles of the ethyl derivative from the crystals of the original substance.

Found %: N 8.68. $C_{20}H_{18}O_3N_2$. Calculated %: N 8.37.

Reductive Acetylation of 2-Amino-3-chloronaphthoquinone. Preparation of 1,4-Diacetoxy-2-acetamino-3-chloronaphthalene. 2.4 g (0.014 g-mole) of 2-amino-3-chloro-1,4-naphthoquinone and 0.1 g of anhydrous sodium acetate were refluxed with 10 ml of acetic anhydride and 1.5 g of zinc dust (added in portions) until the solution was decolorized (about 12 hours). From the solution 3.8 g (90%) of product was separated, with m.p. 154-156°. After two recrystallizations from alcohol – colorless crystalline substance (hexahedral prisms) with m.p. 158-159°. Readily soluble in alcohol or glacial acetic acid.

* In contrast with the sulfonamide derivative, which was insoluble in the usual solvents.

Found %: N 4.18. $C_{16}H_{14}O_5NCl$. Calculated %: N 4.17.

1,4-Diacetoxy-2-p-acetylsulfonamidophenylamino-3-chloronaphthalene was obtained as described above, from 2-p-sulfonamidophenylamino-3-chloro-1,4-naphthoquinone [5] after 5 hour refluxing of the reaction mixture. Yield good, m.p. 138-139° (colorless hexahedral plates, from alcohol). The substance dissolved readily in dilute sodium hydroxide solution; the solution rapidly became rose- colored (saponification and oxidation proceeded more rapidly than for the above- mentioned substance). Upon acidifying the solution, a rose-colored product was precipitated.

Found %: N 5.78. $C_{22}H_{19}O_7N_2ClS$. Calculated %: N 5.94.

1,3,4-Triacetoxy-2-ethylphenylaminonaphthalene. Obtained from 2-ethylphenylamino-3-hydroxynaphthoquinone-1,4 [6] after 6 hour refluxing of the reaction mixture, as described above. From alcohol after several recrystallizations — colorless crystals with m.p. 170-171°, yield 20%. Readily soluble in alcohol or glacial acetic acid.

Found %: N 3.40. $C_{24}H_{23}O_6N$. Calculated %: N 3.46.

SUMMARY

A number of 2,3-substituted derivatives of 1,4-naphthoquinone, not previously described in the literature, have been prepared.

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REACTIONS OF HALOMETAL ALCOHOLATES

VIII. CONTROL OF ORGANOMAGNESIUM REACTIONS

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As a result of previous investigations [1-3] devoted to a study of the reactions of halometal alcoholates with esters, it was in particular established that halomagnesium alcoholates of tertiary aliphatic and aliphatic-aromatic alcohols upon interaction with esters (ethyl formate or diethyl oxalate) are converted to unsaturated hydrocarbons.

However, there remained an unanswered question as to the influence on the course of this reaction exerted by side groups attached to the phenyl or naphthyl radical, especially by those containing atoms of oxygen, nitrogen, sulfur, etc., with their unshared electron pairs. In these cases it is possible to form an additional bond between these elements and the magnesium atom, which has a stabilizing action on the halomagnesium alcoholates, hindering their conversion to unsaturated hydrocarbons.

In order to clarify this question, a study was made of the reaction between esters and halomagnesium alcoholates of tertiary aliphatic-aromatic alcohols containing alkoxy groups on the second or fourth carbon atom of the naphthyl radical.

The properties of the aliphatic-aromatic alcohols which we synthesized for this purpose are listed in Table 1.

In all cases the halomagnesium carbinolates of the alcohols enumerated in the table are converted smoothly (under the action of esters) to unsaturated hydrocarbons (Table 2), which attests to the wider limits of applicability of this reaction.

Since halomagnesium carbinolates are the final products of many organomagnesium reactions, the established fact of their easy convertibility to unsaturated hydrocarbons under the action of esters can be used for control of these reactions.

This possibility was demonstrated in the instance of organomagnesium compounds listed in Table 1, with acetophenone. By the addition of esters (ethyl formate or diethyl oxalate) the reaction was directed toward the formation of unsaturated hydrocarbons instead of tertiary alcohols (Table 3).

EXPERIMENTAL

Synthesis of the tertiary aliphatic-aromatic alcohols (Table 1) was carried out under the usual Grignard reaction conditions. The second component (acetone) was used in 50% excess. Since the bromine derivatives of alkoxynaphthalenes have relatively low solubility in anhydrous ether, the reaction was carried out in ether-benzene (1 : 1) medium. Purification of the material was carried out by recrystallization from petroleum ether.

The general conditions for conducting the reactions between the bromomagnesium carbinolates of the tertiary alcohols and ethyl formate were as follows: To the tertiary alcohol, dissolved in three volumes of anhydrous ether, there was added an ether (three volumes) solution of ethylmagnesium bromide (content of ethylmagnesium bromide

TABLE 1

Interacting components (1:1 1/2)	Name of reaction product*	Yield, %	Melting point (from petroleum ether)	Empirical formula	% C found	% C calculated	% H found	% H calculated	% OH found	% OH calculated	% OR found	% OR calculated
α-Naphthylmagnesium bromide + acetone	Dimethyl-α-naphthylcarbinol	90	80°	$C_{13}H_{14}O$	83.67	83.84	7.51	7.58	9.0	9.1	—	—
2-Methoxy-1-naphthylmagnesium bromide + acetone	Dimethyl-(2-methoxynaphthyl-1)-carbinol	65	93.5	$C_{14}H_{16}O_2$	77.73	77.75	7.38	7.46	7.5	7.9	13.9	14.3
2-Ethoxy-1-naphthylmagnesium bromide + acetone	Dimethyl-(2-ethoxynaphthyl-1)-carbinol	81	84	$C_{15}H_{18}O_2$	78.20	78.23	7.82	7.88	7.2	7.4	18.2	19.6
4-Methoxy-1-naphthylmagnesium bromide + acetone	Dimethyl-(4-methoxynaphthyl-1)-carbinol	96	94.5	$C_{14}H_{16}O_2$	77.57	77.75	7.50	7.46	7.4	7.9	13.6	14.3
4-Ethoxy-1-naphthylmagnesium bromide + acetone	Dimethyl-(4-ethoxynaphthyl-1)-carbinol	95	112	$C_{15}H_{18}O_2$	78.18	78.23	7.90	7.88	7.2	7.4	18.4	19.6

* All of the alcohols synthesized except dimethyl-α-naphthylcarbinol are reported for the first time.

TABLE 2

Interacting components (0.1 g-mole)	Name of reaction product*	Yield, %	Boiling point (pressure in mm)	Empirical formula	% C found	% C calculated	% H found	% H calculated	d_4	n_D	MR_D found	MR_D calculated
MgBr-dimethyl-α-naphthylcarbinolate + ethyl formate	α-Methyl-α-(1-naphthyl)-ethylene	78	118—120° (5)	$C_{13}H_{12}$	92.80	92.86	7.20	7.14	1.0190 (18°)	1.6020 (18°)	56.54	55.03
MgBr-dimethyl-(2-methoxynaphthyl-1)-carbinolate + + ethyl formate	α-Methyl-α-(2-methoxynaphthyl-1)-ethylene	51	128—130 (6)	$C_{14}H_{14}O$	84.74	84.84	7.00	7.07	1.0680 (27°)	1.6050 (27°)	62.95	61.29
MgBr-dimethyl-(2-ethoxynaphthyl-1)-carbinolate + + ethyl formate	α-Methyl-α-(2-ethoxynaphthyl-1)-ethylene	62	133—140 (6)	$C_{15}H_{16}O$	84.90	84.92	7.58	7.54	1.0458 (20°)	1.5717 (20°)	66.65	65.91
MgBr-dimethyl-(4-methoxynaphthyl-1)-carbinolate + + ethyl formate	α-Methyl-α-(4-methoxynaphthyl-1)-ethylene	81	132—134 (6)	$C_{14}H_{14}O$	84.80	84.84	7.10	7.07	1.0980 (25°)	1.6120 (25°)	62.69	61.29
MgBr-dimethyl-(4-ethoxynaphthyl-1)-carbinolate + + ethyl formate	α-Methyl-α-(4-ethoxynaphthyl-1)-ethylene	85	142—144 (6)	$C_{15}H_{16}O$	84.89	84.92	7.49	7.54	1.0630 (20°)	1.5945 (20°)	67.72	65.91

* The unsaturated compounds synthesized, except α-methyl-α-(1-naphthyl)-ethylene, are reported for the first time.

TABLE 3

Interacting components (0.1 g-mole)	Third component added to reaction mixture (0.1 g-mole)	Name of reaction product*	Yield, %	Melting point	Empirical formula	% C		% H	
						found	calculated	found	calculated
α-Naphthylmagnesium bromide + acetophenone	Ethyl formate	α-Phenyl-α-(1-naphthyl)-ethylene	65	60° (from ethanol)	$C_{18}H_{14}$	93.87	93.91	6.10	6.09
2-Methoxy-1-naphthylmagnesium bromide + acetophenone	Ethyl formate	α-Phenyl-α-(2-methoxynaphthyl-1)-ethylene	62	71 (from methanol)	$C_{19}H_{16}O$	87.70	87.68	6.13	6.15
2-Ethoxy-1-naphthylmagnesium bromide + acetophenone	Diethyl oxalate	α-Phenyl-α-(2-ethoxynaphthyl-1)-ethylene	60	58 (from ethanol)	$C_{20}H_{18}O$	87.52	87.59	6.48	6.57
4-Methoxy-1-naphthylmagnesium bromide + acetophenone	Ethyl formate	α-Phenyl-α-(4-methoxynaphthyl-1)-ethylene	62	59.5 (from methanol)	$C_{19}H_{16}O$	87.54	87.68	6.18	6.15
4-Ethoxy-1-naphthylmagnesium bromide + acetophenone	Diethyl oxalate	α-Phenyl-α-(4-ethoxynaphthyl-1)-ethylene	70	85 (from ethanol)	$C_{20}H_{18}O$	87.56	87.59	6.60	6.57

* Except for the α-phenyl-α-(1-naphthyl)-ethylene, the listed unsaturated compounds are reported for the first time.

was determined by titration with hydrochloric acid). To the ether solution of the bromomagnesium carbinolate thus prepared, there was added an equimolecular quantity of ethyl formate, dissolved in an equal volume of anhydrous ether. The reaction mixture was heated 3 hours and decomposed by water and 10% acetic acid. Purification of the reaction product (unsaturated hydrocarbon) was accomplished by vacuum distillation. In view of the tendency of the unsaturated hydrocarbons to polymerize, the first distillation usually left a certain quantity of polymer in the flask.

Control of the reactions between alkoxynaphthylmagnesium bromides and acetophenone, with the aim of obtaining an unsaturated hydrocarbon instead of a carbinol, was carried out as follows: After mixing the ether solution of the organomagnesium compound and the acetophenone, the reaction mixture was heated 1 hour and then an ether solution (1 : 1) of ethyl formate or diethyl oxalate was added to it. The reaction mixture was again heated, this time for 2 hours. After decomposition of the mixture by water and 10% acetic acid, the ether layer was washed with 10% sodium bicarbonate solution and then with water to neutral reaction, the solvent was distilled off, and the reaction product was vacuum distilled and recrystallized from ethanol or methanol.

SUMMARY

1. A study has been made of the reaction between esters (ethyl formate and diethyl oxalate) and halomagnesium alcoholates of tertiary aliphatic-aromatic alcohols containing alkoxy groups connected to the second or fourth carbon atom of the naphthyl radical. It was established that the product of interaction is an unsaturated compound with the same carbon skeleton as in the original tertiary alcohol.

2. The possibility has been established of controlling the reaction between organomagnesium compounds and ketones in the direction of forming unsaturated compounds in place of carbinols.

3. A number of new alkoxy-substituted carbinols and unsaturated compounds have been synthesized; these have not been reported previously in the chemical literature.

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* Original Russian pagination. See C. B. Translation.

REACTIONS OF HALOMETAL ALCOHOLATES

IX. INTERACTION OF ESTERS OF KETO ACIDS WITH HALOMAGNESIUM ALCOHOLATES

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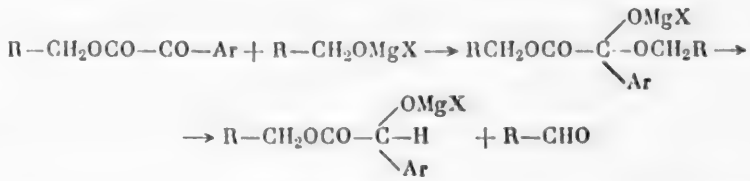
In a series of previous articles [1-3] a method was described for obtaining esters of secondary α-hydroxy acids based on the interaction of arylmagnesium halides with oxalic esters, taken in equimolecular quantities.

A study of the mechanism of this reaction [4] led to establishing the actual cause of the formation of these compounds, namely that the initially formed complex compound, being unstable, is decomposed.

The analogous complex compound which results from the reaction of alkylmagnesium bromides with oxalic esters is more stable; it is decomposed to the same type of products, but only at a higher temperature (110-120°) [5].

Establishing the mechanism of this reaction makes it possible to predict that the interaction of esters of α-keto acids with halomagnesium alcoholates, when there is formed a similar complex compound with the same degree of thermal stability and decomposing according to the same equation, must result in the formation of esters of secondary α-hydroxy acids.



The experimental investigation described in the present article confirms this hypothesis.

Upon heating halomagnesium alcoholates with arylglyoxalic esters in ether solution (b.p. 40-42°) and with alkylglyoxalic esters in toluene (mixture b.p. 115-120°), as a result of reduction, esters of secondary α-hydroxy acids are formed with very high yields, exceeding 90%.

In general, esters of α-keto acids are reduced under exactly the same conditions as those under which esters of α-hydroxy acids are formed from organomagnesium compounds and oxalic esters.

Of the esters of α-keto acids, only esters of the type $ArCH_2COCOOR$, as established in the instance of $C_6H_5CH_2COCOOC_2H_5$, are not reduced by halomagnesium alcoholates either in ether or in toluene solution. In all probability, decomposition of the resulting complex required a high temperature of heating.

Component I	B.p. (P, mm)	Component II	Solvent**	Name of reaction	Yield, %	B.p. (P, mm)	M.p. of α-hydroxy acid obtained by saponification of ester	
							experimental	literature
Ethyl benzoylformate	254° (760) [6]	Chloromagnesium ethoxide; also bromo- and iodomagnesium ethoxide	Ether	Ethyl mandelate	92—97	115° (5)	119—120°	118—119° [7]
n-Butyl benzoylformate	117 (3)	Bromomagnesium n-butoxide	Ether	n-Butyl mandelate	96	120 (3)	119—120	118—119 [7]
Ethyl 2,4,6-trimethylbenzoylformate	164—165 (10) [8]	Bromomagnesium ethoxide	Ether	Ethyl 2,4,6-trimethylmandelate	92	M.p. 52—53	153—154	152—153 [9]
n-Butyl 2,4,6-trimethylbenzoylformate*	153—154 (6)	Bromomagnesium n-butoxide	Ether	n-Butyl 2,4,6-trimethylmandelate	97	M.p. 42	153—154	152—153 [9]
Ethyl isoamyglyoxalate	105 (18) [10]	Bromomagnesium ethoxide	Toluene	Ethyl 2-methylhexane-5-ol-6-carboxylate	91	203 (750)	61—62	60.5 [11]
n-Butyl α-oxocaprate	123 (5)	Bromomagnesium n-butoxide	Toluene	n-Butyl α-hydroxycaprate	93	123—124 (5)	71—72	70.5 [12]

* This experiment was conducted by student Yu. S. Andreichikov. The preparation had d_4^{18} 1.0302, nD^{18} 1.5043.

** Heating 3 hours at refluxing temperature.

In contrast to the esters of α-keto acids, the esters of β-keto acids are not reduced by halomagnesium alcoholates. The products of interaction of these reactants are halomagnesium alcoholates of the enol form of the esters of the β-keto acids.

The complex compound formed by esters of γ-keto acids and halomagnesium alcoholates is stable and is not decomposed at the boiling temperature of the ether solution; this leads (after hydrolysis) to regeneration of the initial ester of the acid.

Under these same conditions, the reduction of the ethyl ester of β-benzoylacrylic acid likewise does not take place; this fact is apparently characteristic in general for esters of acids of the type ArCOCH = CH-COOH.

The results of the investigation are set forth in the table.

Thus, halomagnesium alcoholates are excellent reducing agents for esters of α-keto acids. In this respect they surpass aluminum isopropylate, which is used for reducing esters of these same acids by the Meerwein-Ponndorf method. In addition, the conditions of operation with halomagnesium alcoholates are more convenient than with aluminum alcoholates.

EXPERIMENTAL

The reduction of esters of aromatic α-keto acids to esters of α-hydroxy acids by the action of halomagnesium alcoholates was carried out under such conditions as proved to be general for these reactions.

To the particular alcohol (the same as that forming the keto ester in question) there was added an ether solution (3 volumes) of alkylmagnesium halide, taken in somewhat lower quantity (the content of alkylmagnesium halide in the ether solution was determined by hydrolysis with water and then titration with hydrochloric acid). To the solution of halomagnesium alcoholate thus obtained, there was added half the equivalent quantity of the ester of the α-keto acid (usually 0.2 mole of the alcoholate and 0.1 mole of the ester were taken) dissolved in two volumes of anhydrous ether, and the reaction mixture was refluxed for 3 hours. After decomposition with water and then with 10% acetic acid, the ether layer was washed successively with water, 10% sodium bicarbonate solution, and again with water to neutral reaction, dried with calcined sodium sulfate, and the solvent was distilled off. The ester of α-hydroxy acid remaining in the flask was relatively pure and usually distilled within very narrow temperature limits. Practically complete reduction occurred. The yields indicated in the table were determined by the OH content of the crude product.

For the purpose of identification, the esters of the α-hydroxy acids were saponified with 10% alcoholic KOH.

In reducing the esters of aliphatic α-keto acids, the diethyl ether was replaced by toluene; this was accomplished by adding anhydrous toluene to the reaction mixture and then distilling off the ether. The same refluxing time (3 hours) was used for the toluene solutions.

The reactions between halomagnesium alcoholates and the esters of β- and γ-keto acids were carried out under analogous conditions.

SUMMARY

1. The reaction between halomagnesium alcoholates and esters of α-keto acids has been studied. It was established that the interaction gives the same complex compound which arises from the interaction of organomagnesium compounds with equimolecular quantities of oxalic esters, having the same degree of thermal stability and decomposing upon heating with the formation of aldehydes and halomagnesium alcoholates of esters of secondary α-hydroxy acids. The best conditions have been found for the reduction of esters of aromatic and aliphatic α-keto acids.

2. This method is not applicable to the reduction of esters of β-keto acids (they form halomagnesium alcoholates of the enol form) or of saturated or unsaturated γ-keto acids (the complex compound is not decomposed upon heating in ether solution.

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• Original Russian pagination. See C. B. Translation.

BIPOLAR IONS FORMED DURING DETACHMENT OF A PROTON FROM THE NH GROUP

XV. SULFONIUM COMPOUNDS CONTAINING AN ACYLAMINO GROUP IN THE ORTHO-POSITION TO THE ONIUM ATOM

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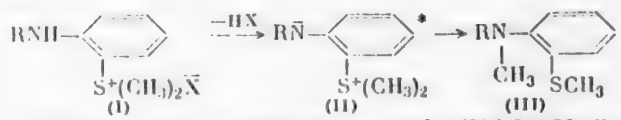
Many examples of conversion of quaternary ammonium salts containing the NH group into bipolar ions (betaines) have already been studied. The conversion has also been described for the sulfonium salts whose structure is analogous [1]. Up to now, however, bipolar ions have not been obtained from onium salts of the aromatic series containing an acylamino group in the ortho position to the onium atom. We therefore synthesized the sulfonium salts (I), established the possibility of converting them to betaines (II), and examined the properties of the latter.



a) R = p-$O_2NC_6H_4SO_2$; b) R = p-$O_2NC_6H_4CO$; c) R = 3,5-$(NO_2)_2C_6H_3CO$; X = $ArSO_3$.

Our experiments showed that salt (Ia) is converted with facility into the bipolar ion (IIa) when an aqueous alcoholic solution of ammonia is added to it. Formation of betaine (IIb) goes with more difficulty: the compound comes down from the solution in low yield when salt (Ib) is treated with concentrated alkali solution. Betaine (IIc) is also formed with relative difficulty. Hence the conversion into bipolar ions of sulfonium salts of structure (I) does not by any means proceed with greater facility than in the case of the para isomers [2]. On this basis we can conclude that the influence of the positively charged sulfur atom, through the inductive effect, on the mobility of the proton in the NH group is small; the mobility is influenced by the acyl, and possibly by the conjugation developed with the dimethylsulfonium group [3].

The properties of the bipolar ions (II) obtained are characteristic of compounds of this class. They are vividly colored and insoluble in nonpolar solvents; with the exception of the 3,5-dinitrobenzoyl derivative, in the fused state they readily undergo the previously described rearrangement [2, 4] to N-methylanilides (III). The structure of the product of rearrangement of betaine (IIa) was confirmed by alternative synthesis.

Rearrangement proceeds equally easily with betaines (II) and their para isomers. The nature of the acyl apparently does not appreciably influence the ease of isomerization. However, if the process is carried out in presence of substances containing a nucleophilic center, the structure of the acyl governs the direction of the conversion. In presence of β-naphthol, only betaine (IIa), containing the acyl of p-nitrobenzenesulfonic acid, undergoes

• Due to redistribution of the electron density, the proton-deficient nitrogen atom bears only part of the anionic charge. In betaine (IIb), for example, the greater part of the charge is in all probability located at the oxygen atom of the CO group.

isomerization. By contrast the bipolar ion (IIb) does not undergo rearrangement but exerts an alkylating action; the products are methyl β-naphthyl ether and the p-nitrobenzoyl derivative of o-thioanisidine. A similar process is observed when β-naphthol is fused with isomeric bipolar ions containing onium and azeniate atoms in the para position.

The differences in behavior of betaines of these two types may be explained in terms of the different degrees of nucleophilicity of the anionic center of the molecule. Nitrobenzoyl derivatives react with β-naphthol with addition of a proton; in consequence the methyl cation attacks the oxygen atom of the naphtholate ion with formation of nerolin (cf. [5]).

$$RC(=O^-)=NC_6H_4\overset{+}{S}(CH_3)_2 + C_{10}H_7OH \rightarrow RC(=O)-NHC_6H_4\overset{+}{S}(CH_3)_2\ |\ \bar{O}C_{10}H_7 \rightarrow$$

$$\rightarrow RC(=O)-NHC_6H_4SCH_3 + C_{10}H_7OCH_3$$

$R = p\text{-}O_2NC_6H_4$.

In the case of nitrobenzoylsulfonyl derivatives, the trimethylarylsulfonium naphtholate is not formed due to the ease of detachment of the proton in the SO_2NH group; therefore the reaction proceeds normally in presence of naphthol, i.e., the betaine isomerizes.

The bipolar ion (IIc) – a derivative of 3,5-dinitrobenzoic acid – could not be made to undergo rearrangement since it broke down when fused.

EXPERIMENTAL

o-Thiomethoxyanilide of 4-nitrobenzenesulfonic acid [o-(4-nitrobenzenesulfamino)-thioanisole]. The compound was prepared by interaction of o-thioanisidine with p-nitrobenzenesulfochloride in pyridine. Pale-yellow plates (from alcohol) with m.p. 158-159°, soluble in benzene, less readily soluble in ether.

Found %: N 8.67, 8.45. $C_{13}H_{12}O_4N_2S_2$. Calculated %: N 8.64.

Dimethyl-[o-(4-nitrobenzenesulfamino)-phenyl]-sulfonium benzenesulfonate (Ia). Yellowish-white, hexagonal plates (from alcohol) with m.p. 182-183°, sparingly soluble in hot water.

Found %: N 5.55, 5.51. $C_{20}H_{20}O_7N_2S_3$. Calculated %: N 5.64.

Dimethyl[o-(4-nitrobenzenesulfamino)-phenyl]-sulfonium betaine (IIa). The compound came down when concentrated aqueous ammonia was added dropwise to an aqueous alcoholic solution of the sulfonium salt at 50-60°. Yellow-brown plates with m.p. 162-163°, easily soluble in dilute acetic acid and dilute mineral acids. Yield 83%.

Found %: N 8.26, 8.28. $C_{14}H_{14}O_4N_2S_2$. Calculated %: N 8.28.

4-Nitrobenzenesulfonic acid N-methyl-o-thiomethoxyanilide [o-(N-methyl-4-nitrobenzenesulfamino)-thioanisole] (IIIa). a) The betaine (0.15 g) was put into a test tube, closed with a stopper to which a calcium chloride tube was attached, and gradually heated on a water bath. At 125-130° the color of the betaine changed to pale-yellow; at about 170° complete fusion took place, and heating was carried out for 5 min at this temperature. After cooling, the light-yellow melt was triturated with a little ether, and the precipitate was filtered off and crystallized from alcohol. Yield 0.14 g. Light-yellow needles with m.p. 168-169°. In contrast to the original betaine, the compound was insoluble in dilute hydrochloric acid and soluble in benzene.

Found %: N 8.07, 8.17. $C_{14}H_{14}O_4N_2S_2$. Calculated %: N 8.28.

Heating of the betaine with the equivalent quantity of β-naphthol gave the isomerization product in 93% yield. Traces of nerolin were formed and could only be detected by odor.*

b) Compound (IIIa) was also obtained by reaction of the 2-thiomethoxyanilide of p-nitrobenzenesulfonic acid with dimethyl sulfate in an alkaline medium. Light-yellow crystals (from alcohol) with m.p. 168-169°. No depression of melting point in admixture with the product of expt. (a).

* Isomerization (95% yield) was likewise the sole process when the isomeric dimethyl-[p-(nitrobenzenesulfamino)-phenyl]-sulfonium betaine was heated.

p-Nitrobenzoic acid o-thiomethoxyanilide [o-(4-nitrobenzoylamino)-thioanisole]. The compound was prepared by reaction of o-thioanisidine with p-nitrobenzoyl chloride in pyridine. Yellowish-white crystals (from alcohol) with m.p. 124-125°, easily soluble in benzene and ether.

Found %: N 9.69, 9.74. $C_{14}H_{12}O_3N_2S$. Calculated %: N 9.72.

Dimethyl-[2-(p-nitrobenzoylamino)-phenyl]-sulfonium toluenesulfonate. Pale-yellow, rhombic plates with m.p. 195-196° (from alcohol).

Found %: N 5.89, 5.83. $C_{22}H_{22}O_6N_2S_2$. Calculated %: N 5.90.

Dimethyl-[o-(4-nitrobenzoylamino)-phenyl]-sulfonium betaine (IIb). Introduction into a warm solution of the sulfonium salt (0.7 g) in very dilute alcohol (25 ml) of 40% sodium hydroxide solution (5 ml) led to separation of golden-red plates. The product was dried in a vacuum desiccator over phosphorus pentoxide; during this operation the color changed to brown-red. Yield 0.07 g with m.p. 130-135°; treatment of the mother liquor with alkali gave a further 0.12 g of product. The compound was soluble in dilute acetic acid, and acetone, rather less easily soluble in alcohol and water.

Found %: N 9.07, 9.01. $C_{15}H_{14}O_3N_2S$. Calculated %: N 9.27.

o-(N-Methyl-4-nitrobenzoylamino)-thioanisole (IIIb). The compound was obtained by isomerization of the betaine at 140°. Yellowish-white needles (from 50% alcohol) with m.p. 135-136°, soluble in benzene, acetone and ether. Yield 83%.

Found %: N 9.46, 9.36. $C_{15}H_{14}O_3N_2S$. Calculated %: N 9.27.

Reaction of dimethyl-[o-(4-nitrobenzoylamino)-phenyl]-sulfonium betaine with β-naphthol. The light-yellow melt obtained by heating 0.12 g of the betaine and 0.07 g (23% excess) of β-naphthol from 125 to 140° was treated (with cooling) with ligroin (three lots of 2 ml each). The insoluble residue was crystallized from alcohol. The resulting pale-yellow leaflets (m.p. 124-125°) were the o-thiomethoxyanilide of p-nitrobenzoic acid. Yield 0.11 g (96%). Colorless crystals of nerolin with m.p. 71-72° were separated from the ligroin and washed with alkali. Yield 0.058 g (92%). Formation of an isomerization product was not detected.

Reaction of dimethyl-[p-(4-nitrobenzoylamino)-phenyl]-sulfonium betaine with β-naphthol. Heating of the betaine [4] with β-naphthol from 125 to 150° gave nerolin (yield 95%) and the 4-thiomethoxyanilide of p-nitrobenzoic acid (yield 90%). A product of rearrangement could not be isolated.

o-Thiomethoxyanilide of 3,5-dinitrobenzoic acid. The compound was prepared from o-thioanisidine and 3,5-dinitrobenzoic acid in benzene in presence of sodium bicarbonate. Yield 80%. Light-yellow needles with m.p. 145-146° (from aqueous acetone), readily soluble in alcohol, ether and acetone, not so soluble in benzene.

Found %: N 12.45, 12.46. $C_{14}H_{11}O_5N_3S$. Calculated %: N 12.61.

Dimethyl-[o-(3,5-dinitrobenzoylamino)-phenyl]-sulfonium betaine (IIc). Dimethyl-o-(3,5-dinitrobenzoylamino)-phenylsulfonium toluenesulfonate, prepared by fusion of the o-thiomethoxyanilide of 3,5-dinitrobenzoic acid with methyl p-toluenesulfonate at 130-140°, was hygroscopic and broke down in aqueous solution at 80°. The solubility of the salt and its stability improve in presence of sodium chloride.

Into a solution of 0.04 g of sodium chloride in 25 ml of alcohol (heated to 75°) was stirred portionwise 0.35 g of the above sulfonium salt. To the warm, light-yellow solution was added 2 ml of 2 N potassium hydroxide, and the red solution was diluted with warm water (20 ml). Brownish-red leaflets came down slowly when the liquid was cooled and triturated with a rod. The precipitate was filtered, washed with water and alcohol, and then dried in a desiccator over phosphorus pentoxide. Yield 0.22 g (96%), m.p. 163-165° (decomp.). Readily soluble in dilute acetic acid.

Found %: N 12.00, 12.38. $C_{15}H_{13}O_5N_3S$. Calculated %: N 12.10.

SUMMARY

1. Sulfonium salts of the aromatic series containing an acylamino group in the ortho position to the sulfonium group were synthesized. The conditions of transformation of these salts into bipolar ions were examined.

2. The betaines in question, containing the radical of p-nitrobenzene-sulfonic acid and p-nitrobenzenesulfonic acid, were isomerized to the N-alkylanilides of these acids.

3. It was shown that heating of these betaines, as well as of their para isomers, with β-naphthol leads to isomerization of the betaine (if the acyl is p-nitrobenzenesulfonyl) or to alkylation of the β-naphthol (if the acyl is p-nitrobenzoyl).

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• Original Russian pagination. See C. B. Translation.

BENZIMIDAZOLE DERIVATIVES

V. THE ACTION OF BASES ON N-ARYLBENZIMIDAZOLIUM SALTS

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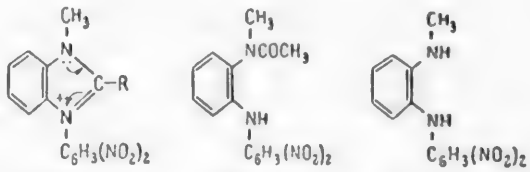
It was earlier shown [1] that the action on a solution of a 1-methyl-3-(2',4'-dinitrophenyl)-benzimidazolium salt (I) of even such a weak base as pyridine leads to formation of 2-(N-formylmethylamino)-2',4'-dinitrophenylamine, which is the amide form of the pseudobase of this salt.• Opening of the dihydroimidazole ring in the unstable cyclic form of the base here proceeds in such a way that the formyl group becomes attached to the nitrogen atom carrying the electropositive radical (methyl). The resulting pseudobase•• -- unlike previously known compounds of this class -- is not reversibly converted by acids into a benzimidazolium salt, while the acyl group is split off on boiling with hydrochloric acid. Similar transformations have been described for some compounds of the purine series [3].

It seemed to us of interest to establish how these reactions proceed in a series of other benzimidazolium salts containing at the imidazole nitrogen an electrophilic group such as phenyl, 2,4-dinitrophenyl and picryl).

Addition of ammonia to an aqueous solution of a 1,2-dimethyl-3-(2',4'-dinitrophenyl)-benzimidazolium salt (II) leads to formation of a brownish-red precipitate of pseudobase. This melts sharply at 168-169° and is insoluble in hydrochloric acid in the cold. Solution occurs only after prolonged boiling; addition of ammonia to the solution until alkaline brings down the previously described [1] 2-methylamino-2',4'-dinitrodiphenylamine (IV). The original pseudobase is smoothly regenerated when acetic anhydride is added. In the light of these reactions we should assign the following structure (III) to the pseudobase.



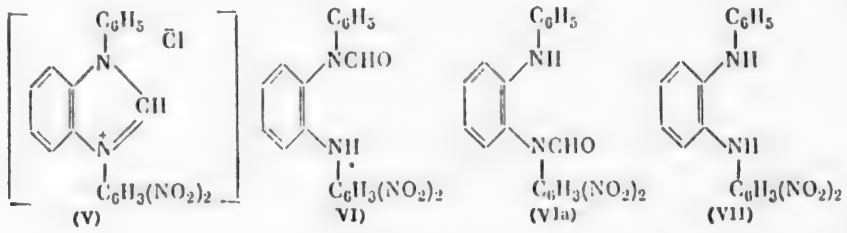
(I) R = H,
(II) R = CH_3.

(III) (IV)

• See [2, 4] in connection with the structure of pseudobases of the benzimidazole series.

•• We arbitrarily retain the name of "pseudobases" for our products of alkaline treatment of N-dinitrophenylbenzimidazolium quaternary salts, although they have lost the characteristic feature of compounds of this class -- the ability to change under the action of acids into the true bases tautomeric with them.

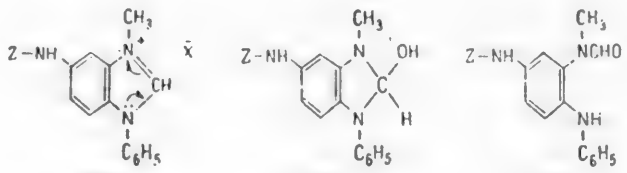
1-Phenylbenzimidazole dinitrophenyl chloride could not be synthesized. The melt obtained by heating an equimolar mixture of 1-phenylbenzimidazole and dinitrochlorobenzene at 100° yielded, after treatment with alcohol in the cold or after trituration with ether, yellow crystals with m.p. 200-201°, insoluble in water and free of chlorine. Analysis of the compound and study of its properties supported the assumption that we had obtained the pseudobase of structure (VI) resulting from hydrolysis of the unstable 1-phenylbenzimidazole dinitrophenyl chloride.



The pseudobase is insoluble in hydrochloric acid and is therefore one of the cyclic forms. It dissolves in alkalies with formation of deeply colored solutions, for which reason we can assign formula (VI) to it and not (VIa), since only (VI) contains a sufficiently labile hydrogen atom to account for its solubility in alkalies. Heating of pseudobase (VI) with concentrated hydrochloric acid leads to deformylation, a red precipitate (m.p. 170-170.5°) being formed which is 2-phenylamino-2',4'-dinitrodiphenylamine (VII).

We also studied the behavior in alkaline media of the 5-p-nitrobenzoylamino-3-methyl-1-phenylbenzimidazolium salt (VIII), prepared by the action of methyl p-toluenesulfonate on 5-p-nitrobenzoylamino-1-phenylbenzimidazole. It was to be expected that, in addition to the pseudobase, a bipolar ion would also be formed since the CONH group contains a labile hydrogen (cf. [4]). However, the orange, crystalline substance (m.p. 197-198°) obtained by the action of dilute sodium carbonate on an aqueous alcoholic solution of salt (VIII) is readily soluble in ether and benzene and is consequently the pseudobase.

The pseudobase soon dissolves when heated with hydrochloric acid to form a colorless solution; on cooling, the latter deposits white crystals with m.p. 299-300°, containing ionogenic chlorine and evidently composed of 5-p-nitrobenzoylamino-3-methyl-1-phenylbenzimidazolium chloride (VIII, X = Cl). This assumption is confirmed by conversion of this compound into benzimidazolium picrate. The latter is identical with the picrate obtained from salt (VIII). Consequently hydrochloric acid does not detach the acyl from the pseudobase — as happens with the pseudobases of salts (I) and (II) — but gives the benzimidazolium salt. In spite of this difference in properties, the pseudobase (IX) is evidently isolated from solution in the amide form and not in the cyclic form (cf. [4]). Since a mixture of isomeric forms is not obtained, the opening of the dihydroimidazole ring in the tautomeric form (IXa) proceeds only in one direction. By analogy with the formation of pseudobases from salts (I) and (III), we can assume that the ring opens round the N atom attached to the electronegative (phenyl) group, and (IXb) is obtained.



Z = p-O2NC6H4CO,
X = p-CH3C6H4SO3

We synthesized 1-picrylbenzimidazole and the 3-methyl-1-picrylbenzimidazolium salt. We failed to obtain the pseudobase by treating the latter with weak alkalies because resinification occurred.

EXPERIMENTAL

2-(N-Acetylmethylamino)-2',4'-dinitrodiphenylamine. a) A solution of 0.5 g of 1,2-dimethyl-3-(2',4'-dinitrophenyl)-benzimidazolium benzenesulfonate [1] in 15 ml of water was gradually treated with 5 ml of ammonia.

The precipitate was filtered and washed with water and alcohol. Yield 0.3 g (90%). Red crystals (from alcohol), m.p. 168-169°, soluble in acetone, insoluble in hydrochloric acid in the cold and after brief heating to 80°. At 125° the red form changes without loss of weight into the yellow form which also melts at 168-169°. The red form can be converted into the yellow form by crystallization from a small volume of acetone.

Found %: N 16.90, 16.92. $C_{15}H_{14}O_5N_4$. Calculated %: N 16.96.

Prolonged (3 hr) refluxing of a suspension of 0.20 g of the compound in 10 ml of 1:1 hydrochloric acid caused the precipitate to dissolve completely. The substance that came down when the solution was made alkaline was crystallized from alcohol. M.p. 178°. No depression in admixture with a specimen of authentic 2-methylamino-2',4'-dinitrodiphenylamine

b) A solution of 0.2 g of 2-methylamino-2',4'-dinitrodiphenylamine in 5 ml of acetic anhydride was heated on a water bath until the red color disappeared (1 hr). It was then cooled, treated with water and neutralized with ammonia. The resulting precipitate was filtered, washed with water and recrystallized from acetone. Yield quantitative. Yellow crystals with m.p. 168°. A mixture with the product of the preceding experiment did not exhibit a depression of melting point.

1-Phenylbenzimidazole was prepared in 75% yield from o-aminodiphenylamine [6] and formic acid. M.p. 96.5°. According to [7] the m.p. is 97°; according to [8] it is 98°.

Picrate: yellow needles (from glacial acetic acid) with m.p. 180-181°.

Found %: N 16.56, 16.62. $C_{13}H_{10}N_2 \cdot HOC_6H_2(NO_2)_3$. Calculated %: N 16.54.

2-(N-Formylphenylamino)-2',4'-dinitrodiphenylamine. A mixture of 1 g of 1-phenylbenzimidazole and 1.1 g of 2,4-dinitrochlorobenzene was melted on a water bath for 2.5 hr. The cooled reddish-brown melt was triturated with alcohol. The resulting precipitate was filtered (the filtrate contained chloride ion) and washed with alcohol. Yield 60%. Yellow prisms (from benzene) with m.p. 200-201°, soluble in alkali with formation of a deeply colored solution; insoluble in ether.

Found %: N 15.05, 14.94. $C_{19}H_{14}O_5N_4$. Calculated %: N 14.81.

2-Phenylamino-2',4'-dinitrodiphenylamine. A solution of 0.1 g of 2-(N-formylphenylamino)-2',4'-dinitrodiphenylamine in 30% alcohol was added to 5 ml of hydrochloric acid solution (d 1.17) and the mixture was refluxed for 15 hr. The precipitate was filtered and washed with water. Yield 0.09 g (90%). Red needles (from alcohol) with m.p. 170-170.5°. According to [5] it has m.p. 170-171°. Soluble in ether and benzene. No melting point depression in admixture with authentic 2-phenylamino-2',4'-dinitrodiphenylamine prepared from N-phenyl-o-phenylenediamine and 2,4'-dinitrochlorobenzene.

5-(p-Nitrobenzoylamino)-1-phenylbenzimidazole. Solutions of 0.5 g of 5-amino-1-phenylbenzimidazole in 15 ml of 30% alcohol, 0.6 g of bicarbonate in 20 ml of water and of 0.57 g of p-nitrobenzoyl chloride (25% excess) in 10 ml of benzene were mixed, and the mixture was shaken until carbon dioxide ceased to come off (2-3 hr). The precipitate was filtered and washed with water and alcohol. Yield 0.72 g (92%). White needles (from a mixture of dioxane and ether) with m.p. 258-259°, soluble in benzene, poorly soluble in ether and alcohol.

Found %: N 15.57, 15.43. $C_{20}H_{14}O_3N_4$. Calculated %: N 15.64.

5-(p-Nitrobenzoylamino)-3-methyl-1-phenylbenzimidazolium p-toluenesulfonate. A mixture of 0.15 g of 5-(p-nitrobenzoylamino)-1-phenylbenzimidazole and 0.1 g of methyl p-toluenesulfonate was fused on a glycerol bath at 160° for 20 min with continuous stirring. The melt was crystallized from alcohol. Yield 0.15 g (66%). White needles with m.p. 263-264°.

Found %: N 10.30, 10.41. $C_{28}H_{24}O_6N_4S$. Calculated %: N 10.29.

5-(p-Nitrobenzoylamino)-3-methyl-1-phenylbenzimidazolium picrate. Prepared by mixing alcoholic solutions of equimolar quantities of 5-(p-nitrobenzoylamino)-3-methyl-1-phenylbenzimidazolium p-toluenesulfonate (or chloride) and picric acid. Yellow needles (from 90% acetic acid) with m.p. 213-214°.

Found %: N 16.12, 15.93. $C_{27}H_{19}O_{10}N_7$. Calculated %: N 16.30.

Pseudobases of 5-(p-nitrobenzoylamino)-3-methyl-1-phenylbenzimidazolium salts. Sodium carbonate solution was added to a warm solution of 0.15 g of 5-(p-nitrobenzoylamino)-3-methyl-1-phenylbenzimidazolium

p-toluenesulfonate in 30% alcohol. A precipitate came down on cooling. Yield 0.1 g (96%). Orange prisms (from aqueous alcohol) with m.p. 197-198°. Soluble in alcohol, ether and acetone, insoluble in water.

Found %: N 14.12, 14.43. $C_{21}H_{18}O_4N_4$. Calculated %: N 14.35.

The compound was dissolved in 25% hydrochloric acid by heating to 90-100°. The precipitate deposited from the cooled solution contained chloride ion. Snow-white needles (from alcohol) with m.p. 299-300°, soluble in water. The original pseudobase separated from the solution when sodium carbonate was added. An alcoholic solution of picric acid gives a picrate identical with 5-p-nitrobenzoylamino-3-methyl-1-phenylbenzimidazolium picrate.

1-Picrylbenzimidazole. A solution of 2.5 g of benzimidazole and 5.3 g of picryl chloride in 15 ml of alcohol was heated on a water bath (50-60°) with shaking. Precipitate ceased to come down after 5-7 min. It was filtered and washed with alcohol. Yield quantitative. Orange-yellow crystals (from alcohol) with m.p. 211-212°, soluble in benzene. The compound resinifies on treatment with caustic alkali in the cold and on heating with weak bases (in alcoholic solutions).

Found %: C 47.25, 47.30; H 2.26, 2.32; N 21.42, 21.31. $C_{13}H_7O_6N_5$. Calculated %: C 47.42; H 2.14; N 21.27.

1-Methyl-3-picrylbenzimidazolium benzenesulfonate. A mixture of 1.5 g of 1-picrylbenzimidazole and 0.8 g of methyl benzenesulfonate was fused at 90° for 4 hr. The cooled melt was triturated with a 3:1 mixture alcohol and ether. The precipitate was filtered and washed with ether. Yield 0.7 g (35%). Greenish-yellow crystals (from alcohol) with m.p. 243-244°, soluble in water. Treatment of the aqueous solution with ammonia and pyridine gave a resinous precipitate which could not be purified.

Found %: N 13.86, 14.05; S 6.52, 6.48. $C_{20}H_{15}O_9N_5S$. Calculated %: N 13.97; S 6.40.

SUMMARY

1. A study was made of the action of weak bases on some quaternary benzimidazolium salts containing an electrophilic radical (phenyl, 2,4-dinitrophenyl, picryl) at the N atom of the imidazole ring.

2. 1-Phenylbenzimidazole is not formed when the stable dinitrophenyl chloride is fused with 2,4-dinitrochlorobenzene. From the melt was isolated the product of its hydrolysis (the pseudobase) — 2-(N-formylphenylamino)-2',4'-dinitrodiphenylamine.

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SYNTHESIS OF ESTERS OF THIOAZOCARBOXYLIC ACIDS

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The only ester of dithioazodicarboxylic acid described in the literature – the di(S-methyl) ester – was synthesized by Arndt by oxidation of the corresponding dithiohydrazo ester with nitric acid [1]. Mixed O,S-dialkyl esters of thioazodicarboxylic acids, likewise esters of tetrathioazodicarboxylic acid, have not previously been investigated. With the objective of partially filling this gap, we now describe a series of O,S-dialkyl esters of thioazodicarboxylic and thiophenylazocarboxylic acids. These esters were synthesized by a modification of the methods of Arndt [1] and Diels [2] according to the following reactions:

$$ROCOCl + NH_2NH_2 \rightarrow ROCONHNH_2 \cdot HCl \quad (I)$$

$$\text{or} \quad (RO)_2CO + NH_2NH_2 \rightarrow ROCONHNH_2$$

$$R'SCOCl + ROCONHNH_2 \rightarrow R'SCONHNHCO_2R \quad (II)$$

$$\text{or} \quad C_6H_5NHNH_2 + R'SCOCl \rightarrow C_6H_5NHNHCOSR'$$

$$R'SCONHNHCO_2R \xrightarrow{HNO_2} R'SCON{=}NCO_2R \quad (III)$$

$$\text{or} \quad C_6H_5NHNHCOSR' \xrightarrow{HNO_2} C_6H_5N{=}NCOSR'$$

The esters of thioazodicarboxylic acid are dark-red liquids. The ethyl esters are much more stable than the methyl. However even the O,S-diethyl ester of thioazodicarboxylic acid breaks down on heating appreciably faster then its oxygen analog. The S-methyl ester of thiophenylazocarboxylic acid is fairly stable during prolonged storage. We planned to synthesized esters of tetrathioazodicarboxylic acid from the disodium salt of hydrazine-bis-dithiocarbonic acid (previously described by us [3]).

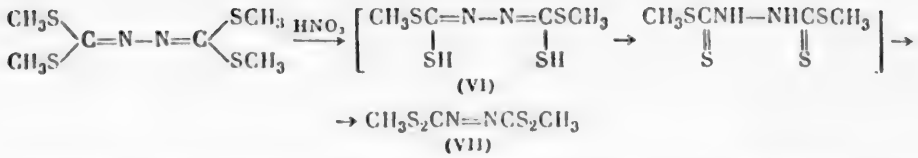
$$NaS_2CNHNHCS_2Na \rightarrow RS_2CNHNHCS_2R \rightarrow RS_2CN{=}NCS_2R$$
$$\text{(IV)}$$

$$NaS_2CNHNHCS_2Na \rightarrow (RS)_2C{=}N{-}N{=}C(SR)_2$$
$$\text{(V)}$$

It was found, however, that alkylation of this salt with dimethyl sulfate did not give the expected ester (IV) but the symm. tetramethyl derivative (V), evidently due to the susceptibility of the original salt to tautomerism.

$$NaSC(=S)NHNHC(=S)SNa \rightleftarrows NaSC(SH){=}N{-}N{=}C(SH)SNa$$

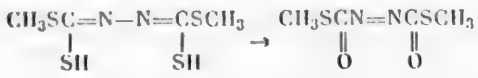
According to [4] the S-alkyl derivatives of cyclic azines are easily saponified by mineral acids; it could therefore be expected that (V) would be converted by nitric acid into the anticipated tetrathio derivative (VII).



(VI)

(VII)

An azo compound was indeed obtained by the action of nitric acid, but was identified as the di-(S-methyl) ester of dithioazodicarboxylic acid.



A similar replacement of thionic sulfur by oxygen during oxidation of thioamides of hydrazodicarboxylic acid has been observed [5].

The infrared spectrum of the O,S-diethyl ester of thioazodicarboxylic acid was compared with the spectra of the ethyl, isopropyl• and butyl esters of azodicarboxylic acid and the spectrum of the ethyl ester of phenylazocarboxylic acid. Unlike the latter, the spectrum of the thioester in question contains two strong absorption bands in the C = O bond region at 5.75 and 5.95 μ (1740 and 1680 cm^{-1}), whereas the C = O frequency in the azodicarboxylic and phenylazocarboxylic esters is in the 5.65 to 5.75 μ region (1770 to 1740 cm^{-1}). The slight shift of the carbonyl group band in comparison with the azocarboxylic esters and the appearance of a second band with a 90 cm^{-1} lower frequency are fully consistent with the nature of the influence on this frequency of the neighboring alkthiol group. The frequency of the C–O ester bond in all of the investigated azo compounds is nearly constant: 8.0-8.1 μ (1250-1235 cm^{-1}).

In addition to the strong absorption bands, all of the azo compounds in question exhibit three bands at 10.65-10.75μ (940-930 cm^{-1}), 9.1μ (1100 cm^{-1}), and 7.65-7.70μ (1305-1300 cm^{-1}), substantially coinciding with the C-N bond vibrations in aromatic azo compounds [6, 7].

It is not without interest to note that the infrared spectra of the above esters of azodicarboxylic and phenylazocarboxylic acids always contain two medium-strong absorption bands at 6.75-6.95μ (1480-1440 cm^{-1}) and at 7.25-7.35μ (1380-1360 cm^{-1}), i.e., in the regions assigned to the absorption bands of the N = N group in aromatic azo compounds [6, 7]. It is not yet clear whether these bands are associated with the valence vibrations of the N = N bond or are due exclusively to the presence of the CH_3-C and CH_2 groups in the compounds concerned, as suggested by Le Fèvre et al., [8].

EXPERIMENTAL

1. Preparation of O,S-dimethyl ester of thiohydrazinedicarboxylic acid $CH_3SCONHNHCO_2CH_3$. To 14 g of methyl hydrazinecarboxylate hydrochloride, dissolved in 200 ml of aqueous alkali (12.5 g KOH) was added 12.5 g of the S-methyl ester of thiochlorocarbonic acid dropwise with cooling and vigorous stirring. The mixture was then stirred for another 2 hr and diluted with 200 ml of cold water. There was obtained 18 g of colorless crystals with m.p. 148° (from water). Yield 98% of theory, calculated on the methyl ester of the chlorocarbonic acid.

Found %: C 28.64, 28.75; H 4.05, 4.38; N 16.94, 16.80. $C_4H_8O_3N_2S$. Calculated %: C 29.22; H 4.88; N 17.05.

2. Preparation of O,S-dimethyl ester of thioazodicarboxylic acid $CH_3SCON = NCO_2CH_3$. To 5 g of the O,S-dimethyl ester of thiohydrazinedicarboxylic acid in 35 ml of ether was added 30 ml of 30% HNO_3. As soon as the reaction became violent, 100 ml of water was added to the mixture. The ethereal layer was separated, washed with water and dried over calcium chloride. The main bulk of solvent was evaporated in vacuo. The azo compound was then frozen out many times from small quantities of ether (fresh ether for each freezing step) cooled with carbon dioxide. The residues of ether were taken off in vacuo. The compound is unstable and was stored in carbon dioxide. Yield 2 g (40%).

• This ester was first synthesized by S. A. Rodkin. The authors thank him for putting the preparation at their disposal.

d_4^{20} 1.180, nD^{20} 1.4518. MR_D 37.1; Calc. 37.58.

Found %: C 28.64, 28.54; H 3.87, 3.60; N 16.81, 16.67. M 160.9. $C_4H_6O_3N_2S$. Calculated %: C 29.62; H 3.70; N 17.27. M 162.16.

3. Preparation of the O-ethyl, S-methyl ester of thiohydrazine dicarboxylic acid $CH_3SCONHNHCO_2C_2H_5$. Preparation was carried out as in expt. 1, starting from 150 g of ethyl hydrazinecarboxylate and 80 g of the S-methyl ester of thiochlorocarbonic acid. Yield 120 g (92%) of product with m.p. 93° (from water).

Found %: C 33.28, 33.55; H 4.59, 4.62; N 14.66, 14.64; S 17.55, 17.33. $C_5H_{10}O_3N_2S$. Calculated %: C 33.70; H 5.62; N 15.73; S 17.95.

4. Preparation of O-ethyl, S-methyl ester of thioazodicarboxylic acid $CH_3SCON = NCO_2C_2H_5$. Preparation as in expt. 2 from 50 g of O-ethyl, S-methyl ester of thiohydrazinedicarboxylic acid. Fractional distillation of the ether extract gave 39.6 g (80%) of azoester with b.p. 120° at 6 mm.

d_4^{20} 1.202, nD^{20} 1.4835, MR_D 41.94; Calc. 42.19.

Found %: C 33.40, 33.05; H 4.12, 3.90; N 14.13, 14.09; S 19.46, 19.33. M 177.2. $C_5H_8O_3N_2S$. Calculated %: C 34.04; H 4.55; N 15.91; S 18.20, M 176.19.

5. Preparation of O,S-diethyl ester of thiohydrazinedicarboxylic acid $C_2H_5SCONHNHCO_2C_2H_5$. From 100 g of ethyl hydrazinedicarboxylate and 60 g of S-ethyl thiochlorocarbonate, by the procedure of expt. 1, was obtained an oil which crystallized after cooling with ice for a few hours. Yield of ester 110 g (95%) with m.p. 44° (dried in desiccator).

Found %: C 37.28, 37.23; H 6.04, 5.90; N 13.54, 13.58; S 15.86, 15.87. $C_6H_{12}O_3N_2S$. Calculated %: C 37.50; H 6.25; N 14.57; S 16.66.

6. Preparation of O,S-diethyl thioazodicarboxylate $C_2H_5SCON = NCO_2C_2H_5$. Oxidation of 50 g of O,S-diethyl thiohydrazinedicarboxylate (see expt. 4) gave 42 g (85%) of azo compound with b.p. 127° at 3 mm.

d_4^{20} 1.157, nD^{20} 1.4755, MR_D 46.4, Calc. 46.81.

Found %: C 38.91, 38.53; H 5.13, 4.55; N 14.22, 14.37; S 15.08, 15.72. M 188. $C_6H_{10}O_3N_2S$. Calculated %: C 37.91; H 5.26; N 14.73; S 16.85. M 190.22.

7. Preparation of S-methyl thiophenylhydrazinecarboxylate $CH_3SCONHNHC_6H_5$. Into an ice-cooled solution of 30.7 g of S-methyl thiochlorocarbonate in 25 ml of alcohol was stirred portionwise a solution of 30 g of phenylhydrazine in 25 ml of alcohol; solid sodium hydroxide was then added to the reaction mass until it gave a permanent coloration with phenolphthalein. After an hour the reaction mass was poured into 200 ml of water, and the crystalline product was recrystallized from alcohol. Yield of ester 45.5 g (90% calculated on the ester of thiochlorocarbonic acid); m.p. 98°.

Found %: N 14.74, 14.78; S 17.04, 17.01. $C_8H_{10}ON_2S$. Calculated %: N 15.55; S 17.70.

8. Preparation of S-methyl ester of thiophenylazocarboxylic acid $CH_3SCON = NC_6H_5$. Oxidation of the hydrazo ester to azo ester was effected as described above with introduction into the reaction mass of 1-1.5 ml of fuming nitric acid. Fractional distillation of the ethereal extract, obtained during oxidation of 40 g of the hydrazo derivative, gave 25.5 g (65%) of azo compound with b.p. 132° at 2 mm. It crystallized when kept (m.p. 32-35°).

Found %: C 53.52, 53.82; H 4.75, 5.27; N 15.45, 15.50; S 17.34, 17.47. $C_8H_8ON_2S$. Calculated %: C 53.40; H 4.45; N 15.54; S 17.75.

9. Preparation of tetra-(S-methyl)-formazine $(CH_3S)_2C = N - N = C(SCH_3)_2$. To a solution of 80 g of disodium salt of hydrazinebisdithiocarbonic acid in 200 ml of water was added 140 ml of dimethyl sulfate dropwise with ice cooling and stirring. After completion of the exothermic reaction, 300 ml of alcohol was added. The deposited crystals were collected, washed with 100 ml of alcohol, and dried in the air. There was obtained 40 g of azine with m.p. 112°. Yield 50%, calculated on the salt taken.

Found %: C 30.50, 30.12; H 4.65, 4.25; N 11.46, 11.30; S 52.56, 52.55. $C_6H_{12}N_2S_4$. Calculated %: C 30.0; H 4.0; N 11.70; S 53.30.

10. Oxidation of tetra-(S-methyl)-formazine with nitric acid. Preparation of the S-dimethyl ester of dithioazodicarboxylic acid $CH_3SCON = NCOSCH_3$. Oxidation was effected by the procedure for oxidation of hydrazoesters described above. From 10 g of azine, after evaporation of the ethereal extract and recrystallization of the azo compound from ligroine, was obtained 3 g (40%) of needles with m.p. 69°. A mixture with authentic ester prepared as in [1] did not exhibit a depression of melting point.

Found %: C 27.04, 27.80; H 4.06, 4.39; N 14.68, 14.70; S 36.60, 36.28. $C_4H_6O_2N_2S_2$. Calculated %: C 26.95; H 3.38; N 15.70; S 36.0.

SUMMARY

1. Oxidation of esters of thiohydrazinedicarboxylic and thiophenylhydrazinecarboxylic acids with nitric acid gave a series of previously undescribed O,S-esters (methyl, ethyl and mixed) of thioazodicarboxylic and thiophenylazocarboxylic acids.

2. Alkylation of the disodium salt of hydrazine-bisdithiocarbonic acid by dimethyl sulfate gave symm. tetra-(S-methyl)-formazine, which oxidized to the S-dimethyl ester of dithioazodicarboxylic acid.

3. The infrared spectra of a series of esters of azodicarboxylic and thioazodicarboxylic acids were studied.

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SYNTHESIS OF SOME DIPHENYLAMINOCARBOXYLIC ACIDS

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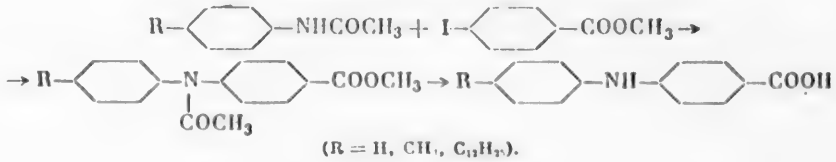
Diphenylamine-3- and -4-carboxylic acids have hitherto been relatively difficultly accessible compounds. The methyl ester of diphenylamine-4-carboxylic acid was prepared by phenylation of the ester of p-aminobenzoic acid with iodobenzene, but the yield was only 27% [1]. Our experiments have shown that this reaction gives a mixture of methyl esters of diphenylamine- and triphenylamine-4-carboxylic acids whose separation is associated with considerable losses (the yield of pure diphenylamine-4-carboxylic acid is 13%).

Reaction of m- and p-iodobenzoic [2] and m-bromobenzoic [3] acids with aniline gave 3-carboxydiphenylamine in a yield of 7 and 35%, and of 4-carboxy derivative in a yield of 15%. Reaction of iodobenzene with m- and p-aminobenzoic acids goes even less smoothly (yield of 4%) [2]. Diphenylamine-3- or -4-carboxylic acid could not be isolated when bromobenzene was the arylating agent or when m- and p-chlorobenzoic acids were reacted with aniline [2, 4].

Preparation of diphenylamine-4-carboxylic acid from 4-acetyldiphenylamine [3] or by the action of phenylmagnesium bromide on nitrobenzoic ester [5] is likewise not very convenient.

In view of the ease of formation of derivatives of triphenylamine on arylation of aromatic amines or aminocarboxylic acids, it might be thought that preparation of diphenylaminemono- and dicarboxylic acids would necessitate the use of a compound containing a substituted amino group. We therefore investigated the reaction of iodobenzene with esters of acetaminobenzoic, phthalic and isophthalic acids, as well as reactions of acetylated aromatic amines with esters of iodo-substituted aromatic acids (see [4, 6, 7]). It was found that esters of m- and p-acetaminobenzoic acids react fairly easily with iodobenzene at 220° (in presence of nitrobenzene, copper and potassium carbonate), and that subsequent hydrolysis of the reaction products gave diphenylamine-3- and -4-carboxylic acids in yields of 55 and 81% respectively. Under similar conditions the dimethyl esters of 5-acetaminoisophthalic and 4-acetaminophthalic acids gave us the previously undescribed diphenylamine-3,5- and 3,4-dicarboxylic acids (yields of 98 and 50% respectively).

Arylation of acetanilide and its p-alkyl derivatives with methyl p-iodobenzoate (in presence of copper and potassium carbonate) also went fairly smoothly; in this manner diphenylamine-4-carboxylic acid (yield 55%) and its 4'-methyl- and 4-dodecyl derivatives (yields 66 and 68%) could be synthesized.



(R = H, CH_3, $C_{12}H_{25}$).

This reaction goes much less satisfactorily with esters of halodicarboxylic acids. In the same way the phenylation of p-acetaminoacetophenone with iodobenzene gave N-acetyl-p-acetyldiphenylamine, identical with the product of reaction of N-acetyldiphenylamine with acetyl chloride (in presence of aluminum chloride), but its hydrolysis gave p-acetyldiphenylamine (cf. [3]). Phenylation with iodobenzene of p-aminoacetophenone and dimethyl 5-aminoisophthalate gave, as was to be expected, the corresponding triphenylamino derivatives in addition to p-acetyldiphenylamine and diphenylamino-3,5-dicarboxylic acid.

EXPERIMENTAL

Diphenylamine-4-carboxylic acid. a) A mixture of 6.21 g of ethyl p-acetaminobenzoate, 31 g of iodobenzene, 8.3 g of anhydrous potassium carbonate, 1 g of copper powder and 30 ml of nitrobenzene was refluxed in a flask over Wood alloy at a bath temperature of 225-230° for 15 hr. The excess of iodobenzene and nitrobenzene was distilled off with steam, the residue was filtered and the filtrate acidified with hydrochloric acid. The separated substance gradually crystallized. The crystals were filtered and mixed with 100 ml of 10% sodium hydroxide solution, and the solution boiled for 1.5 hr. The filtered solution was acidified with hydrochloric acid, and the resulting precipitate washed with water and dried. Yield 5.2 g (81.3%). M.p. 149-153°. After crystallization from benzene it had m.p. 159-160°. Literature [8] m.p. 159-160°.

b) A mixture of 10.48 g of methyl p-iodobenzoate, 5.68 g of acetanilide, 6.8 g of anhydrous potassium carbonate and 1.6 g of copper powder was refluxed in a flask on a bath of Wood alloy at 205-210° (bath temperature) for 15 hr. The reaction mass was extracted with ether, the ether was driven off, and the residue distilled with steam for removal of unreacted methyl p-iodobenzoate. The water was decanted from the residual oily product, 100 ml of 10% potassium hydroxide solution was added, and the mixture boiled for 1.5 hr. The aniline formed was then distilled off with steam. The residue was acidified with acetic acid, and the resulting crystals filtered, washed with water and dried. Weight 2.36 g, m.p. 156°. The solid product, remaining after treatment of the reaction mass with ether, was dissolved in water with heating. The solution was filtered and acidified with acetic acid, the precipitate was filtered and mixed with 30 ml of 10% potassium hydroxide solution; the resulting solution was boiled for 1.5 hr. The potassium salt of diphenylamine-4-carboxylic acid came down on cooling and was washed with 10% potassium hydroxide solution; it was then dissolved in water and the solution acidified with hydrochloric acid. The precipitate was filtered, washed with water and dried. Weight 2.36 g, m.p. 156°. Total yield of diphenylamine-4-carboxylic acid 4.72 g (55.4%). The compound obtained by both methods did not give the qualitative reaction for triphenylamine derivatives (blue color with sulfuric acid).

Methyl ester. A solution of 10.65 g of diphenylamine-4-carboxylic acid in 55 ml of anhydrous methyl alcohol was saturated at room temperature with dry hydrogen chloride for 3 hr. The next day the solution was boiled for 2 hr and cooled. The precipitate was filtered, washed with water, with 5% sodium carbonate solution and again with water. Yield 10.3 g (90.7%), grayish crystals with m.p. 113-115°. After purification by chromatography over aluminum oxide in benzene solution, the yield was 10.1 g (approx. 89%). Colorless prisms with m.p. 115-116°. After crystallization from methanol the m.p. was 116°. Literature [2] m.p. 115-116°.

4'-Methyldiphenylamine-4-carboxylic acid. A mixture of 10.48 g of methyl p-iodobenzoate, 6.26 g of acetyl-p-toluidine, 1.6 g of copper powder and 6.8 g of anhydrous potassium carbonate was heated for 15 hr under the conditions specified above. The products were isolated in the manner described for diphenylamine-4-carboxylic acid. Yield 6.0 g (approx. 66.1%), m.p. 180-181°. Colorless prisms with m.p. 183° (from methanol).

Found %: N 6.28. $C_{14}H_{13}O_2N$. Calculated %: N 6.16.

The methyl ester was prepared in similar fashion to the methyl ester of diphenylamine-4-carboxylic acid. The yield after chromatography on alumina in benzene solution was 80%; m.p. 122-125°. After crystallization from alcohol the yield was 74.1%. Colorless prisms with m.p. 125°.

Found %: N 5.74. $C_{15}H_{15}O_2N$. Calculated %: N 5.80.

4'-n-Dodecyldiphenylamine-4-carboxylic acid. A mixture of 26.2 g of methyl p-iodobenzoate, 31.8 g of p-dodecylacetanilide, 17 g of anhydrous potassium carbonate, 4 g of copper powder and 100 ml of nitrobenzene was refluxed in a flask on a bath of Wood alloy at 210-215° (bath temperature) for 15 hr. The reaction mass was diluted with ether (about 300 ml) and the precipitate filtered and washed with ether. The residue after distillation of the ether was steam-distilled for removal of nitrobenzene and unreacted methyl p-iodobenzoate, and

subsequently distilled under reduced pressure for removal of water. To the oily residue was added a solution of 22 g of potassium hydroxide in 240 ml of 50% alcohol, and the solution was boiled for 3 hr. The potassium salt came down when the solution was cooled; it was filtered and washed with 30-40 ml of 10% potassium hydroxide solution, and then heated with 150 ml of diluted (1 : 1) hydrochloric acid on a boiling water bath for 10 min. The free acid was then filtered off, washed with water, dried and crystallized from methanol. Yield 26 g (68.2%), m.p. 144-146°. Recrystallization gave colorless tablets with m.p. 146-147°.

Found %: N 3.70. $C_{25}H_{35}O_2N$. Calculated %: N 3.66.

Methyl ester. A warm solution of 9.5 g of 4'-n-dodecyldiphenylamino-4-carboxylic acid in 400 ml of anhydrous methanol (prepared by boiling) was saturated with dry hydrogen chloride (3 hr). The next day the solution was boiled for 2 hr and cooled. The precipitate was filtered, washed with sodium carbonate solution, then with water, and dried. Yield 9.84 g, m.p. 77-80°. After crystallization from methanol the yield was 8.15 g (82.8%). Colorless prisms with m.p. 81-82°.

Found %: N 3.57. $C_{26}H_{37}O_2N$. Calculated %: N 3.53.

Diphenylamine-3-carboxylic acid. A mixture of 5.79 g of methyl m-acetaminobenzoate, 35 g of iodobenzene, 8.3 g of anhydrous potassium carbonate, 1 g of copper powder and 40 ml of nitrobenzene was heated at 220-230° for 15 hr. The product was isolated by the procedure described for diphenylamine-4-carboxylic acid. After crystallization from water the yield of diphenylamine-3-carboxylic acid was 3.55 g (about 55.6%). Colorless needles with m.p. 140-141°. Literature: m.p. 141-142° [2]; 140° [9].

Methyl m-acetaminobenzoate. Prepared by boiling a mixture of 9.06 g methyl m-aminobenzoate, 40 ml glacial acetic acid and 12 g of acetic anhydride for 3 hr. The product was separated from the reaction mass with water. Yield 70.8% (from benzene). Colorless prisms with m.p. 136°.

Found %: N 7.48. $C_{10}H_{11}O_3N$. Calculated %: N 7.24.

Diphenylamine-3,5-dicarboxylic acid. A mixture of 10 g of dimethyl 5-acetaminoisophthalate, 50 g of iodobenzene, 11 g of potassium carbonate, 1 g of copper powder, 0.5 g of potassium iodide and 30 ml of nitrobenzene was heated on a bath of Wood alloy at 230-235° (bath temperature) for 17 hr. The excess of iodobenzene and nitrobenzene was distilled off with steam. To the residue (approx. 80 ml) was added 10 g of potassium hydroxide. The mixture was boiled for 4 hr, and the solution was filtered, cooled and acidified with dilute hydrochloric acid. The precipitated yellowish crystals were washed with water and dried. Yield 10.05 g (97.7%), m.p. 289-290°. The compound did not give a blue coloration with sulfuric acid. Crystallization from 80% acetic acid gave faintly yellowish crystals with m.p. 297-298°. The solution in sulfuric acid turned violet when nitric acid was added.

Found %: N 5.51. $C_{14}H_{11}O_4N$. Calculated %: N 5.44.

The dimethyl ester was prepared by a method similar to that employed for the ester of diphenylamine-4-carboxylic acid. After purification by chromatography on alumina in benzene solution, the yield was 62.3%. After one crystallization from methanol the yield was 47.6%, m.p. 140-141°. Slightly yellowish, rectangular plates.

Found %: N 4.98. $C_{16}H_{15}O_4N$. Calculated %: N 4.91.

Diphenylamine-3,4-dicarboxylic acid. Prepared similarly to the 3,4-derivative, starting from the dimethyl ester of 4-acetaminophthalic acid (yield 51%). Yellowish prisms from glacial acetic acid with m.p. 192-193°. Easily soluble in aqueous alkalies, alcohol and acetic acid, insoluble in water.

Found %: N 5.36. $C_{14}H_{11}O_4N$. Calculated %: N 5.44.

The dimethyl ester was obtained like the methyl ester of diphenylamine-4-carboxylic acid. The product separated as a dark oil after cooling and neutralization of the reaction mixture with 20% sodium carbonate solution. Chromatography (in benzene) gave a light-yellow oil which gradually crystallized. Yield 76.7%. Crystallization from gasoline (b.p. 60-90°) gave colorless crystals with m.p. 85-86°.

Found %: N 5.10. $C_{16}H_{15}O_4N$. Calculated %: N 4.91.

3,5-Dicarbomethoxytriphenylamine. A mixture of 0.57 g of 3,5-dicarbomethoxydiphenylamine, 3 g of iodobenzene, 0.56 g of potassium carbonate, 0.02 g of potassium iodide, 0.04 g of copper powder and 1.7 ml of nitrobenzene was heated on a bath of Wood alloy at 220° (bath temperature) for 4 hr. After the mass had been

steam-distilled, the residue was extracted with ether. The ethereal solution was dried with potassium carbonate and the ether distilled off. Yield 0.32 g (44.4%). Slightly yellowish crystals with m.p. 138-142°. After two crystallizations from methanol the m.p. was 150°. Colorless, equilateral prisms. The product imparts a blue color to sulfuric acid.

Found %: N 3.95. $C_{22}H_{19}O_4N$. Calculated %: N 3.87.

p-Acetyl-n-acetyldiphenylamine. a) A mixture of 3.6 g of p-acetylaminoacetophenone,• 24.4 g of iodobenzene, 5.5 g of anhydrous potassium carbonate, 0.4 g of copper powder and 20 ml of nitrobenzene was heated (at a bath temperature of 200-205°) for 15 hr. The reaction mass was diluted with 40 ml of ether and filtered from the precipitate, which was washed with ether. After the ether had been distilled off, likewise the iodobenzene and nitrobenzene (with steam), the precipitated product was filtered, washed with water, and (for removal of acetylaminoacetophenone) treated with 200 ml of water at the boil (in two portions). The product crystallized after cooling. It was filtered, dried (weight 3.6 g, m.p. 92-94°), purified by chromatography over alumina in benzene solution, and crystallized from gasoline (b.p. 80-90°). Yield 1.84 g (36.3%), m.p. 119-122°. Colorless crystals with m.p. 121-122°. Literature [3]: m.p. 124°.

Found %: N 5.29. $C_{16}H_{15}O_2N$. Calculated %: N 5.52.

b) To a solution of 5.25 g of N-acetyldiphenylamine in 9 ml of carbon disulfide was added 5 g of acetyl chloride and then 11.65 g of aluminum chloride in small portions. The reaction mass was heated on a boiling water bath for 6 hr and cooled; 2 ml of hydrochloric acid (d 1.19) and ice were then added. The oily product was extracted with carbon disulfide, and the extract washed with water and dried with sodium sulfate. After removal of the carbon disulfide, the residue was triturated with 5 ml of ether, filtered, washed with 3-4 ml of ether (weight 1 g, m.p. 104-117°), and crystallized from gasoline. Yield 0.54 g (8.5%), m.p. 121-122°. No depression of melting point in admixture with the product of reaction of p-acetaminoacetophenone with iodobenzene.

p-Acetyldiphenylamine. a) A mixture of 12.15 g of p-aminoacetophenone, 36.7 g of iodobenzene, 12.42 g of potassium carbonate, 1.8 g of copper powder and 70 ml of nitrobenzene was heated at 190-195° (bath temperature) for 15 hr. The thick, brownish mass was filtered; the precipitate was washed with ether which was then added to the filtrate. Steam distillation of the latter removed the ether, nitrobenzene and excess of iodobenzene. The oily residue crystallized when rubbed in presence of dilute hydrochloric acid (1:1). The precipitate was filtered, washed with water, dried and extracted at the boil with 180 ml of gasoline (until crystals ceased to come down when the solution was cooled). Weight 6.25 g, m.p. 92-95°; after crystallization from gasoline the yield was 3.4 g (17.9%), m.p. 106-108°. Slightly yellowish prisms (from methanol or gasoline) with m.p. 112°. Literature [3]: m.p. 112°.

Found %: C 79.33; H 6.24; N 6.61. $C_{14}H_{13}ON$. Calculated %: C 79.59; H 6.20; N 6.62.

Evaporation of the gasoline mother liquors yielded 3.8 g of p-acetyltriphenylamine with m.p. 137-138°. Crystallization from methanol gave yellowish crystals with m.p. 139-140°.

Found %: C 83.76; H 5.85; N 4.73. $C_{20}H_{17}ON$. Calculated %: C 83.59; H 5.96; N 4.87.

b) A mixture of 2.76 g of N-acetyl-p-acetyldiphenylamine and 60 ml of 15% hydrochloric acid was boiled for 1.5 hr in a flask with a reflux condenser. The mixture was cooled and the crystals filtered off and washed with water. The product was triturated with 5% sodium carbonate solution, filtered, washed with water (weight 2.2 g, m.p. 96-98°) and crystallized from gasoline. Yield 1.1 g (47.7%), m.p. 105-108°. Recrystallization gave yellowish prisms with m.p. 111-112°; no depression in admixture with the p-acetyldiphenylamine obtained by the preceding method.

SUMMARY

1. A study was made of the arylation with iodobenzene of esters of m- and p-acetaminobenzoic, phthalic and isophthalic acids and of p-acetaminoacetophenone, also of the arylation by the ester of p-iodobenzoic acid of acetanilide and its p-alkyl derivatives followed by hydrolysis of the resulting compounds.

2. It was shown that these methods can give satisfactory yields of diphenylamine-3- and -4-monocarboxylic acids, of corresponding 3,4- and 3,5-dicarboxylic acids, and also of p-acetyldiphenylamine free of derivatives of triphenylamine.

• Prepared in 60% yield by reaction of acetanilide with acetyl chloride in carbon disulfide in presence of aluminum chloride [10].

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STUDIES IN THE FIELD OF THE SYNTHESIS OF DI-QUATERNARY SALTS OF N, N'-DERIVATIVES OF HEXAMETHYLENE DIAMINE

I. THE SYNTHESIS OF HEXAMETHYLENE-1,6-BIS-DI-METHYL AMINOACETIC ACID AND ITS ESTERS

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Quaternary ammonium compounds of various structures have found wide practical use as bactericidal preparations [1], therapeutic compounds [2, 3], cation active substances [4], sensitizers and desensitizers, pigment fixers, etc.

The di-quaternary compounds are no less important, especially derivatives of hexamethylene diamine. Hexamethylene diamine itself and its derivatives have been studied chiefly for the purpose of investigating polycondensations [5, 6] and the synthesis of N-monoalkyl derivatives and N, N'-dialkyl derivatives [7].

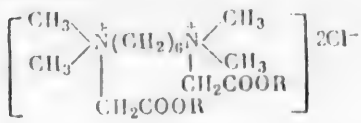
In recent decades the attention of investigators has been attracted to di-quaternary salts of hexamethylene diamine derivatives, hexonium, hexonium B and others [8-11] which are used in medicine.

In order to study biological action we have synthesized di-quaternary derivatives of hexamethylenediamine from monochloroacetic acid and its esters. We started from hexamethylene diamine, from which we obtained hexamethylene-1,6-bis-dimethylamine by the method described in the literature [12]. Hexamethylene-bis-dimethylamine has a strongly basic character [7] and therefore easily reacts with haloesters of the aliphatic series, a fact which we have utilized in the synthesis. We showed that esters of monochloroacetic acid with a high molecular weight react with hexamethylene bis-dimethylamine the more slowly, the longer the carbon chain of the alkyl group, and that the normal structure reacts more easily than the iso-structure. We used a two stage process to obtain the di-quaternary salts of hexamethylene-1,6-bis-dimethylaminoacetic acid and its esters. Starting from hexamethylene diamine, formalin, and formic acid we obtained hexamethylene-1,6-bis-dimethylamine [11], which was isolated from the resulting formate by NaOH solution.

$$H_2N(CH_2)_6NH_2 + 4CH_2O + 6HCOOH \rightarrow (CH_3)_2N(CH_2)_6N(CH_3)_2 \cdot 2HCOOH + 4CO_2 + 4H_2O$$
$$(CH_3)_2N(CH_2)_6N(CH_3)_2 \cdot 2HCOOH + 2NaOH \rightarrow (CH_3)_2N(CH_2)_6N(CH_3)_2 + 2HCOONa + 2H_2O$$

In the second stage hexamethylene-1,6-bis-dimethylamine acted on the ester of monochloroacetic acid. The reaction was run in a medium of anhydrous ether. The di-quaternary salt precipitated as a white, crystalline mass. Thus we synthesized the di-quaternary salts of hexamethylene-1,6-bis-dimethylaminoacetic acid and its dimethyl, diethyl, di-n-propyl, diisopropyl, di-n-butyl, diisobutyl, di-n-amyl, and diisoamyl esters, whose structure and properties are given in the table.

Properties of the Dichlorides of Hexamethylene-1,6-bis-dimethylaminoacetic Acid and Its Esters



Empirical formula	R	M.p.	Yield (in %) on starting tertiary diamine	% N		% Cl	
				found	calculated	found	calculated
$C_{14}H_{30}O_4N_2Cl_2$	H	159—160°	80	7.50, 7.58	7.75	19.1, 19.2	19.63
$C_{16}H_{34}O_4N_2Cl_2$	CH_3	106—108	95	7.15, 7.10	7.19	18.0, 18.1	18.21
$C_{18}H_{38}O_4N_2Cl_2$	C_2H_5	116—118	96.5	6.91, 6.92	6.71	16.63, 16.65	16.99
$C_{20}H_{42}O_4N_2Cl_2$	n-C_3H_7	126—128	98	6.19, 6.20	6.29	15.78, 15.88	15.92
$C_{20}H_{42}O_4N_2Cl_2$	iso-C_3H_7	106—108	98	6.09, 6.15	6.29	15.83, 15.85	15.92
$C_{22}H_{46}O_4N_2Cl_2$	n-C_4H_9	136—138	97	6.01, 5.99	5.94	14.96, 15.30	14.98
$C_{22}H_{46}O_4N_2Cl_2$	iso-C_4H_7	162	96.9	5.72, 5.80	5.94	15.17, 15.00	14.98
$C_{24}H_{50}O_4N_2Cl_2$	n-C_5H_{11}	146—148	95	5.38, 5.45	5.58	14.08, 14.09	14.14
$C_{24}H_{50}O_4N_2Cl_2$	iso-C_5H_{11}	110—112	96	5.40, 5.48	5.58	14.10, 14.10	14.14

R = H, CH_3, C_2H_5, n—C_3H_7, iso C_3H_7, n-C_4H_9, iso-C_4H_9, n-C_5H_{11}, iso-C_5H_{11}.

All these compounds are white, crystalline, hygroscopic substances, very soluble in water, less so in alcohol, insoluble in ether, benzene, and acetone.

In the series of resulting di-quaternary salts the esters with normal structure showed an increase in melting point of about 10° with increase in molecular weight due to advance to the next homolog.

EXPERIMENTAL

Hexamethylene-1,6-bis-dimethylaminoacetic acid dichloride. Twenty-one g of monochloroacetic acid was mixed with 60.5 g of sodium acetate ($CH_3COONa \cdot 3H_2O$) at room temperature. To the resulting mixture, with energetic stirring, was gradually added 17.2 g of hexamethylene-1,6-bis-dimethylamine. Then the reaction mixture was heated on a water bath to 80° for 30 minutes, after which 15 ml of water was added and 1 g of sodium bicarbonate; heating was continued for 30 minutes more. The cooled reaction mass was acidified with hydrochloric acid to a strongly acid reaction. The solution was evaporated dry on a water bath. The dry residue was treated with anhydrous alcohol, the crystals of NaCl were filtered off and the product from the filtrate was precipitated with absolute ether. After two reprecipitations the resulting substance had the physical properties shown in the table.

Dimethyl hexamethylene-1,6-bis-dimethylaminoacetate dichloride. A solution of 0.05 mole of hexamethylene-1,6-bis-dimethylamine in absolute ether (1 : 2) was added gradually with energetic stirring to 0.11 mole of methyl monochloroacetate mixed with absolute ether (1 : 1). A white, crystalline mass formed at once. The reaction mixture stood for a day at room temperature. Then the reaction product was filtered off, washed three times with absolute ether, and was twice recrystallized from anhydrous alcohol by precipitation with absolute ether.

The remaining compounds of this series were obtained in an analogous way.

SUMMARY

1. We have synthesized for the first time hexamethylene-1,6-bis-dimethylaminoacetic acid dichloride.

2. We have studied the reaction of hexamethylene-1,6-bis-dimethylamine with esters of monochloroacetic acid. We have obtained eight new dichlorides of dialkyl hexamethylene-1,6-bis-dimethylaminoacetate.

3. With increase in the size of the alkyl radicals in the ester series their chemical reactivity with hexamethylene-1,6-bis-dimethylamine decreases.

4. We have shown that in the series of the resulting di-quaternary salts of the above-mentioned esters with normal structure with increase in molecular weight between two homologs the melting point increases by about 10°.

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THIAZOLINE-4-CARBOXYLIC ACID AND ITS DERIVATIVES

IX. THE CONDENSATIONS OF N-ACETYLDIMETHYLCYSTEINE WITH COMPOUNDS WHICH HAVE AN ALDEHYDE FUNCTION

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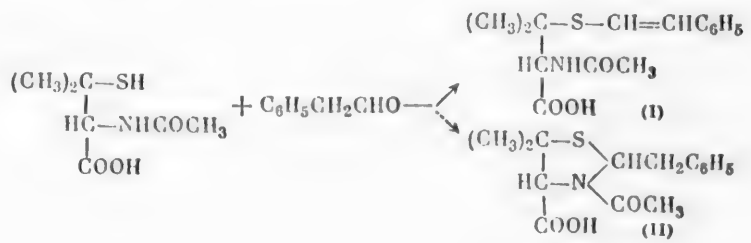
One of the ideas suggested for the synthesis of penicillin was that the thiazolidine and β-lactam rings be closed at the same time, using various N-penaldylpenicillamines or their acetals [1-3]. The latter were heated without catalysts or in their presence, to liberate the aldehyde function from the acetal, but in no case was penicillin obtained, although in some experiments the reaction mass had weak antibiotic activity [1].

It is possible that penicillin under these conditions either was not obtained at all or was inactivated as an unstable compound. Also, no compounds were isolated which would permit following the conversion of the acetal of N-penaldylpenicillamine when it was heated under different conditions.

On this basis the investigators came to believe that aldehydes react with difficulty with β-mercapto-α-acylamino acids [1]. However, I. L. Knunyants and co-workers were able to show that N-acetyldimethylcysteine easily reacted with benzaldehyde in dioxane saturated with dry hydrogen chloride and they obtained in good yield 2-phenyl-5,5-dimethylthiazolidine-4-carboxylic acid [4].

These contradictory results induced us to make a further study of the reaction of N-acetyldimethylcysteine with aldehydes. It is fully acceptable theoretically that compounds with aldehyde groups should react differently with β-mercapto-α-acylamino acids depending on the mobility of the hydrogen on the carbon atom next to the aldehyde group. With limited mobility of the hydrogen, thiazolidine compounds (II) can be formed, and in the contrary case, β-S-vinyl substituted β-mercapto α-acylamino acids (I). Benzaldehyde in this case is exceptional, since in it there is no hydrogen atom on the carbon next to the aldehyde group.

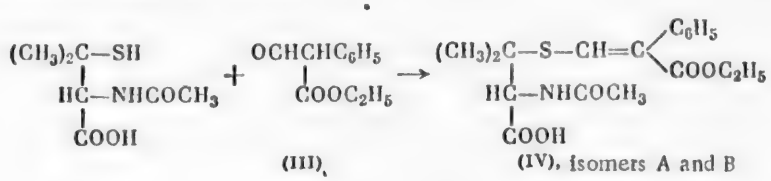
To test this suggestion, we took phenylacetaldehyde, in which there is a good mobility of the hydrogen atom in the CH_2 group. In its reaction with N-acetyldimethylcysteine in dioxane saturated with dry hydrogen chloride we obtained β-S-styryl-N-acetyldimethylcysteine (I).



The isomeric 2-benzyl-3-acetyl-5,5-dimethylthiazolidine-4-carboxylic acid (II) was prepared from dimethylcysteine hydrobromide and phenylacetaldehyde with later acetylation of the 2-benzyl-5,5-dimethylthiazolidine-4-carboxylic acid by acetic anhydride.

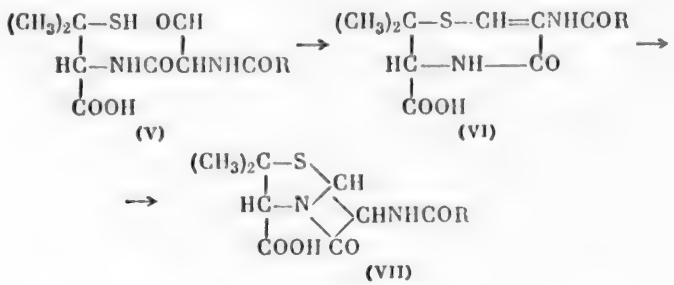
Compounds (I) and (II) differ in their physical properties: the first melts at 144-146°, the second at 174-175°. They have different ultraviolet spectra. In the spectrum of β-S-styryl-N-acetyldimethylcysteine (I) with a conjugated double bond with the phenyl group there is a band λ_{max} 296 mμ (lg ε 4.2), while the isomeric compound (II) has a band λ_{max} at 260 mμ (lg ε 2.4). In the infrared spectrum of β-S-styryl-N-acetyldimethylcysteine there is an absorption band at 1562 cm^{-1}, which is characteristic for SCH = CHC_6H_5 groupings, while in the spectrum of the thiazolidine compound this band is absent.

N-Acetyldimethylcysteine also reacts easily with ethyl formylphenylacetate (III) in dioxane saturated with dry hydrogen chloride. Due to the differing solubilities of the sodium salts we isolated from the reaction mass two compounds with melting points 153-154° and 154-155°. They were not identical since their mixture showed a considerable depression. Their infrared spectra had the absorption band 1567 cm^{-1}, characteristic for the SCH = CHC_6H_5 group. On this basis the compounds can be considered spatial isomers of β-S-(α-phenyl-α-carbethoxyvinyl)-N-acetyldimethylcysteine (IV, compounds A and B).



(III) (IV), isomers A and B

It remains to explain whether S-vinyl substituted N-acetyldimethylcysteines can be converted by heating to the corresponding thiazolidine compounds, as occurs in S-vinyl substituted cysteine [5]. A solution of this question on a simple model compound was of great interest for work on the transformation of N-penaldylpenicillamine (V) into penicillin (VII) through the corresponding 1,4-thiazepine (VI), where R is a group characteristic of penicillins.



(V) (VI) (VII)

For this purpose β-S-styryl-N-acetyldimethylcysteine and β-S-(α-phenyl-α-carbethoxyvinyl)-N-acetyldimethylcysteine (isomers A and B) were heated in an inert solvent. However, the hydrogen of the amide group had very weak mobility and evidently for this reason could not form the thiazolidine ring.

Thus, the prospects for obtaining penicillins from unsaturated thiazepine compounds seem unlikely.

EXPERIMENTAL

β-S-Styryl-N-acetyldimethylcysteine (I). To 1 g of N-acetyldimethylcysteine and 1 g of freshly distilled phenylacetaldehyde was added 5 ml of dioxane saturated with dry hydrogen chloride. On the next day the mass was diluted with 50 ml of water and extracted with ether. The substance was extracted from the ether solution by a solution of sodium bicarbonate. The aqueous solution was acidified with hydrochloric acid and the oil which precipitated was again removed with ether and after drying with magnesium sulfate, the ether was removed. To the residue was added 8 ml of toluene and it remained for several days for crystallization. The resulting colorless

crystals were recrystallized several times from toluene. Prisms with m.p. 144-146°. The substance was soluble in ether, alcohol, acetone, ethyl acetate, and chloroform, insoluble in benzine.

Found %: C 61.68; H 6.50; N 4.97; S 11.05. $C_{15}H_{19}O_3NS$. Calculated %: C 61.42; H 6.53; N 4.77; S 10.91.

We boiled 0.2 g of β-S-styryl-N-acetyldimethylcysteine with 4 ml of dry toluene for 15 hours. The toluene was distilled off to 1 ml and the residue crystallized in the refrigerator. The colorless crystals were filtered off. Weight 0.15 g, m.p. 144-146°. A mixture with the starting compound showed no depression.

2-Benzyl-5,5-dimethylthiazolidine-4-carboxylic acid. One g of dimethylcysteine hydrobromide was dissolved in 3 ml of water and we added 0.36 g of sodium acetate, 0.6 g of freshly distilled phenylacetaldehyde, and heated for one hour on a boiling water bath. After cooling, we extracted the reaction mass with ether and then extracted the resulting compound from the ether with a solution of sodium bicarbonate. After acidification of the water solution with hydrochloric acid to a weakly acid reaction the precipitate was separated, dried, and recrystallized from alcohol. M.p. 125-127°. The substance was soluble in ether, alcohol, acetone, ethyl acetate and poorly soluble in chloroform and toluene.

Found %: C 61.35; H 6.93; N 5.52. $C_{13}H_{17}O_2NS$. Calculated %: C 62.10; H 6.81; N 5.57.

2-Benzyl-3-acetyl-5,5-dimethylthiazolidine-4-carboxylic acid (II). We dissolved 0.35 g of 2-benzyl-5,5-dimethylthiazolidine-4-carboxylic acid in 5 ml of pyridine, added 1 ml of acetic anhydride, and allowed the mixture to stand until the next day. The reaction mass was diluted with 30 ml of water, acidified with 20% sulfuric acid and the substance which separated was extracted with ether. The solution was washed with water, dried over magnesium sulfate, and the ether distilled off. Colorless crystals remained which were recrystallized from a small amount of toluene. Prisms with m.p. 174-175°. The substance was soluble in ether, alcohol, acetone, and ethyl acetate, more poorly so in chloroform and toluene.

Found %: C 61.11; H 6.60; N 4.87. $C_{15}H_{19}O_3NS$. Calculated %: C 61.42; H 6.53; N 4.77.

β-S-(α-Phenyl-α-carbethoxyvinyl)-N-acetyldimethylcysteine (IV). To 1 g of N-acetyldimethylcysteine and 1.72 g of ethyl formylphenylacetate was added 5 ml of dioxane saturated with dry hydrochloric acid, and after shaking, the mixture stood until next day. The reaction mass was diluted with water and extracted with ether. The upper layer was separated, washed with water, and the substance extracted with a solution of sodium bicarbonate. A sodium salt slowly crystallized from the water solution. After several days it was filtered off, washed with cold water and the precipitate dissolved in warm water and the solution was acidified with hydrochloric acid. The oil which precipitated quickly crystallized. Weight 0.85 g. The substance was recrystallized several times from a mixture of acetone with ether. Needles, m.p. 153-154°. Compound (A) was soluble in alcohol, acetone, ethyl acetate, and chloroform, very poorly soluble in ether and benzene.

Found %: C 59.07, 59.01; H 6.23, 6.14; N 3.91; S 8.80. $C_{18}H_{23}O_5NS$. Calculated %: C 59.17; H 6.34; N 3.83; S 8.80.

We boiled 0.3 g of β-S-(α-phenyl-α-carbethoxyvinyl)-N-acetyldimethylcysteine (compound A) with 10 ml of dry toluene for 5 hours. When it cooled in the refrigerator over night, we isolated a colorless crystalline precipitate (0.28 g). After recrystallization from acetone with ether we obtained 0.25 g of substance with m.p. 154-155° which gave no depression when mixed with the starting compound.

The mother liquor after filtration of the poorly water soluble sodium salt was acidified with hydrochloric acid and the substance which separated was extracted with ether. The solution was washed with water, dried with sodium sulfate, and the ether distilled off. There remained 1.1 g of a colorless, crystalline substance which was recrystallized several times from a mixture of acetone and ether. Prisms with m.p. 154-155°. Substance (B) was soluble in alcohol, acetone, ethyl acetate, and chloroform, poorly soluble in ether and toluene.

Found %: C 59.24; H 6.37; N 3.70; S 8.75. $C_{18}H_{23}O_5NS$. Calculated %: C 59.17; H 6.34; N 3.83; S 8.80.

A mixture of compounds (A) and (B) melted at 137-138°.

Compound (B) underwent no change when heated with toluene.

SUMMARY

We have obtained β-S-styryl-N-acetyldimethylcysteine and β-S-(α-phenyl-α-carbethoxyvinyl)-N-acetyl-dimethylcysteine. These compounds could not be converted into the corresponding isomeric thiazolidine compounds.

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SPATIAL STRUCTURE AND REACTIVITY

XVII. THE REACTION OF ATOMIC GROUPS SEPARATED FROM EACH OTHER AS SHOWN BY STUDIES OF REACTION KINETICS OF AMINO DERIVATIVES OF DIPHENYLAMINE AND AZOBENZENE WITH p-NITROBENZOYL CHLORIDE AND PICRYL CHLORIDE

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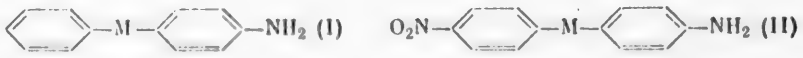
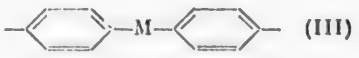
In a number of previous communications [1-6] data have been presented on the study of reaction kinetics in benzene for p-nitrobenzoyl chloride and picryl chloride with amino derivatives which have the structures (I) and (II).



M is either a hydrocarbon bridge grouping (-CH_2-, -CH_2-CH_2-, -CH = CH-, -C ≡ C-, etc.) or a bridge of heteroatoms (-O- or -S-).

It was found that the ability to transmit the effect of a nitro group on the rate of acylation of the amino group in a molecular system of the form



(III)

could be more or less quantitatively characterized by the ratio of rate constants for the reactions of mono and disubstituted derivatives, for example K_I/K_{II} (factor f).

In the present communication we give data on the study of the kinetics of analogous reactions in the series of amino derivatives of diphenylamine (M = -NH-) and trans-azobenzene (M = -N=N-) under conditions entirely identical with those preceding, which permits us to explain the nature of the transfer of the effect of the substituent from one benzene ring to the other in a molecular system of type (III) in the case of compounds of these rings with nitrogen-containing bridges.

EXPERIMENTAL

I. Preparation and Purification of Starting Substance

Benzene, p-nitrobenzoyl chloride [7], and picryl chloride [4] were purified as described before.

4-Aminodiphenylamine (I, M= -NH-). A commercial product ("pure") was recrystallized once as the hydrochloride from dilute hydrochloric acid (1 : 2) with activated charcoal. The salt was ground with a cold aqueous solution of ammonia; the free base thus obtained was washed with water and twice recrystallized from alcohol with activated charcoal. This operation had to be carried out as fast as possible, because when the alcohol solution was allowed to stand, it became colored. After two recrystallizations from a mixture of benzene and ligroin (1 : 2) and vacuum drying for three hours at 35°, the product was colorless (or light rose colored) and had m.p. 75.5-76° (according to [8], 75°).

4-Amino-4'-nitrodiphenylamine (II, M= -NH-) was obtained by the method described in the literature [9]. The unpurified product (red color) was dissolved in a mixture of benzene and acetone (2 : 1) and chromatographed on aluminum oxide. The main fraction of the amine was washed out with the same mixture of solvents from which, after partial evaporation, a yellow precipitate separated, with m.p. 204-205°. It was recrystallized from alcohol. It is interesting that from the still-warm alcohol solution there precipitated also yellow crystals with m.p. 205-207° which, under this solution, gradually over several hours changed to a red form with m.p. 212-213°.• After recrystallization from benzene the melting point of the red crystals did not change (in the literature [10] this form is reported with m.p. 212°). Evidently the yellow form is a metastable polymorphic modification of 4-amino-4'-nitrodiphenylamine.

Trans-4-aminoazobenzene (I, M= -N=N-). A commercial preparation ("pure") was recrystallized twice as the salt from a mixture consisting of different volumes of water, glacial acetic acid, and concentrated hydrochloric acid. The hydrochloride was ground with concentrated ammonia solution and was converted to the free base which was then twice recrystallized, first from alcohol, and then from benzene. After drying in a vacuum for three hours at 100°, it melted at 126°, which agreed with the literature [11].

Trans-4-amino-4'-nitroazobenzene (II, M= -N=N-) was prepared by the described method [12]. The substance was purified from the accompanying tarry impurities by passing its toluene solution through a column of aluminum oxide. The product which was isolated by evaporation of the toluene was dissolved in boiling alcohol and boiling water was added to the solution to the formation of a stable turbidity. The crystals of the amine which separated after the solution had stood for 12 hours were recrystallized two or three times as the salt from the same mixture of acids and water as the 4-aminoazobenzene. The free base obtained from the hydrochloride by grinding with ammonia was dark red and was twice recrystallized from benzene. After drying in a vacuum for four hours at 100° it melted at 217°.

II. Methods of Kinetic Measurements and Results

The methods of calculating the second order rate constants, Arrhenius energy of activation (E_A), frequency factor (A) and entropy of activation ($\Delta S^{\#}$) were described before [13]. For measurement of the rate of reaction of the amino derivatives of azobenzene with p-nitrobenzoyl chloride and picryl chloride we used the earlier described method [1] according to which the aromatic amino group was determined by potentiometric titration with sodium nitrite. In the case of the amino derivatives of diphenylamine, this method was unsuitable, since both 4-aminodiphenylamine and its 4'-nitro derivative in the nitrite titration after rapid reaction with an equimolecular amount of nitrous acid then slowly reacted with a further amount of HNO_2 (probably because of reaction with the -NH- group), which made quantitative calculation difficult. Therefore, in measuring the rate of reaction of the 4-amino derivatives of diphenylamine we used another method, which was the following.

The working solutions of amine and picryl chloride (20 ml each), as in measuring the rate by the first method, were poured into the same flask with a ground-glass stopper. Reaction was stopped here by pouring into the mixture of reacting substances 8-10 ml of 0.1 N nitric acid. After energetic mixing of the contents of the flask for one minute they were poured into a separatory funnel. Then 10 ml of distilled water was added, the mixture was shaken energetically, and the water layer was separated. The benzene layer was extracted four times more using 10 ml of water each time, and the flask in which the reaction took place was rinsed with the first portions. To the combined extracts was added the mixed indicator [14] (diphenyl carbazone + bromphenyl blue) and after bringing the solution as recommended [14] to a corresponding pH, the chloride ion was determined by titration with 0.01 N $Hg(NO_3)_2$. In order to determine the amount of $Hg(NO_3)_2$ used by chloride contained in the form of

• If after chromatography the product was recrystallized as the hydrochloride from dilute (1 : 3) hydrochloric acid and the hydrochloride was decomposed with a hot concentrated ammonia solution and then recrystallized from alcohol, we obtained at once the red product with m.p. 212-213°.

TABLE 1

Reaction Rate Constants of Some Amines with Picryl Chloride at Different Dilutions

Amine	a (m)	b (m)	k_{25}, liter/mole · sec
4-Aminodiphenylamine	0.000625	0.00125	2.98
	0.00125	0.0025	2.85
4-Amino-4'-nitrodiphenylamine	0.000625	0.00125	0.0689
	0.0004167	0.002083	0.0660
4-Aminoazobenzene	0.00833	0.01667	0.00214
	0.005	0.01	0.00202

impurities in the water and reagents, we always ran a parallel control experiment which repeated all the conditions of the above experiment, but instead of the working solutions of picryl chloride we used pure benzene. In the case of the reaction of 4-amino-4'-nitrodiphenylamine this was especially important, since the solution of the salt of the amine was colored.

Before each series of kinetic measurements it was advisable to ascertain the reliability of the prepared working solutions of picryl chloride and amine, for which purpose a mixture of the reacting components either in molecular ratio 1 : 2, or with a somewhat greater amount of amine, was kept for such a period of time that the reaction was known to be completely ended. In this case 100% completion of the reaction was shown by the absence of side processes and by correct analytical controls. Finally, we tested the accuracy of the method by measuring the rate of the earlier studied reaction of picryl chloride with 4-amino-biphenyl where we used the ordinary method of stopping the reaction by diethylamine and carried out the diazometric determination of the amine. Here we obtained results which agreed well: k_{25}• by the previous (diazometric) method was 0.0744 and according to the new results (mercurimetric method) 0.0781 liter/mole • second.

The reaction rates of 4-amino derivatives of diphenylamine with p-nitrobenzoyl chloride were so rapid that it was difficult to measure them. The reaction with picryl chloride also proceeded very rapidly; therefore the measurement of the rate here was possible only with considerable dilution of the reacting components.

In all the main experiments the initial concentration of p-nitrobenzoyl chloride or picryl chloride (a) was always half the initial concentration of the amine (b). Several experiments carried out at different initial concentrations of the reagents showed that the rate constants of the studied reactions were practically unchanged with dilution, as the data of Table 1 indicate. In the case of the reaction of 4-amino derivatives of diphenylamine we can expect that picryl chloride will react not only with the primary, but with the secondary amino group. It was shown by control measurements that under the conditions of the kinetic experiments for 4-aminodiphenylamine and 4-amino-4'-nitrodiphenylamine, diphenylamine itself did not react to any considerable extent with picryl chloride even after 48 hours.• The reaction of 4-aminodiphenylamine with these reagents at 25° occurs to the extent of about 70% in 10 minutes, when a = 0.000625 and b = 0.00125, or in 4 minutes at a = 0.00125 and b = 0.0025. The fact that side reactions in our case did not play a practically important role indicates that, as already mentioned, the rate constants do not depend on dilution and are practically unchanged by the course of the reaction.

The reaction between 4-amino-4'-nitroazobenzene and picryl chloride was sufficiently slow. We could not increase its rate by increasing the concentration of reacting components•• because of the slight solubility of

• When the benzene solutions of diphenylamine and picryl chloride were poured together there was no visible change in color, which indicates the absence under these conditions of the formation of a molecular compound between these substances (cf. [15] and [16]).

•• In order to work with the maximum concentration of reacting substances pouring of the working solutions of amine and picryl chloride was carried out not in equal volumes, but in such a way that to 1 ml of benzene solution of picryl chloride with a concentration of 0.05 M was added 5 ml of a solution of amine with concentration of 0.02 M.

TABLE 2

Kinetics of the Course of the Reaction of 4-Aminodiphenylamine with Picryl Chloride
a = 0.000625 mole, b = 0.00125 mole

25°				10°			
t_i (in min)	yield (in %)	k_i (liter/ /moles · sec)	n_i	t_i (in min)	yield (in %)	k_i (liter/ / moles · sec)	n_i
2	31.9	3.15	2	3	26.6	1.59	2
3	40.6	3.06	2	5	36.7	1.53	2
5	52.1	2.92	2	7	45.6	1.58	2
7	60.9	2.99	2	10	54.4	1.57	2
10	67.3	2.76	2	15	62.6	1.47	2
$k_{25°} = 2.98 \pm 0.09$				$k_{10°} = 1.55 \pm 0.04$			

E_A = 7300 cal/ mole; lg A = 5.83; ΔS# = -33.8 cal/ deg · mole

TABLE 3

Kinetics of Reaction of 4-Amino-4'-Nitrodiphenylamine with Picryl Chloride
a = 0.000625 mole, b = 0.00125 mole

25°				50°			
t_i (in min)	yield (in %)	k_i (liter/ / moles · sec)	n_i	t_i (in min)	yield (in %)	k_i (liter/ / moles · sec)	n_i
50	21.2	0.0723	2	15	19.3	0.220	2
90	31.4	0.0682	2	33	34.1	0.217	2
120	37.6	0.0673	2	50	44.0	0.217	2
180	48.0	0.0687	2	75	52.9	0.207	2
300	60.4	0.0681	2	115	63.6	0.210	2
$k_{25°} = 0.0689 \pm 0.0017$				$k_{50°} = 0.214 \pm 0.004$			

E_A = 8700 cal/ mole; lg A = 5.20; ΔS# = -36.8 cal/ deg . mole

TABLE 4

Kinetics of Reaction of 4-Aminoazobenzene with p-Nitrobenzoyl Chloride
a = 0.005 mole, b = 0.01 mole

25°				50°			
t_i (in min)	yield (in %)	k_i (liter/ / moles · sec)	n_i	t_i (in min)	yield (in %)	k_i (liter/ / moles · sec)	n_i
37	20.9	0.0120	2	13	21.5	0.0365	2
60	29.7	0.0118	2	20	29.6	0.0364	3
93	41.1	0.0126	2	40	45.7	0.0364	3
140	49.0	0.0115	2	57	54.2	0.0358	2
210	60.8	0.0124	2	85	64.4	0.0368	3
$k_{25°} = 0.0121 \pm 0.0003$				$k_{50°} = 0.0364 \pm 0.0008$			

E_A = 8400 cal/ mole; lg A = 4.27; ΔS# = -41.1 cal/ deg · mole

TABLE 5

Kinetics of Reaction of 4-Amino-4'-Nitroazobenzene with p-Nitrobenzoyl Chloride
a = 0.005 mole, b = 0.01 mole

25°				50°			
t_i (in min)	yield (in %)	k_i (liter/ / mole·sec)	n_i	t_i (in min)	yield (in %)	k_i (liter/ / mole·sec)	n_i
180	19.2	0.00222	2	67	20.9	0.00680	2
340	31.6	0.00228	2	115	31.1	0.00678	2
530	43.3	0.00242	2	180	41.5	0.00681	2
				270	52.7	0.00712	2
				420	63.4	0.00711	2
$k_{25°} = 0.00231 \pm 0.00009$				$k_{50°} = 0.00692 \pm 0.00016$			

E_A = 8400 cal/mole; lg A = 3.52; $\Delta S^{\#}$ = -44.5 cal/deg·mole

TABLE 6

Kinetics of Reaction of 4-Aminoazobenzene with Picryl Chloride
a = 0.00833 mole, b = 0.01666 mole

25°				50°			
t_i (in min)	yield (in %)	k_i (liter/ / mole·sec)	n_i	t_i (in min)	yield (in %)	k_i (liter/ / mole·sec)	n_i
90	16.6	0.00223	2	30	21.5	0.00947	2
180	27.1	0.00208	2	48	31.1	0.00973	2
330	41.0	0.00212	2	75	41.3	0.00972	2
500	51.4	0.00213	2	110	51.3	0.00992	2
750	61.3	0.00213	2	170	60.4	0.00929	2
$k_{25°} = 0.00214 \pm 0.00005$				$k_{50°} = 0.00963 \pm 0.00019$			

E_A = 11500 cal/mole; lg A = 5.77; $\Delta S^{\#}$ = -34.2 cal/deg·mole

TABLE 7

Kinetics of Reaction of 4-Amino-4'-Nitroazobenzene with Picryl Chloride
a = 0.00833 mole, b = 0.01666 mole

50°				70°			
t_i (in min)	yield (in %)	k_i (liter/ / mole·sec)	n_i	t_i (in min)	yield (in %)	k_i (liter/ / mole·sec)	n_i
123	14.8	0.00146	2	66	19.6	0.00391	3
240	24.1	0.00137	2	120	30.3	0.00385	2
400	32.9	0.00127	2	196	41.7	0.00387	2
720	45.7	0.00121	2	290	51.4	0.00387	2
1080	57.0	0.00127	2	440	60.0	0.00362	2
$k_{50°} = 0.00132 \pm 0.00006$				$k_{70°} = 0.00383 \pm 0.00009$			

E_A = 11700 cal/mole; lg A = 5.06; $\Delta S^{\#}$ = -37.6 cal/deg·mole

TABLE 8

Combined Data on Reaction Kinetics of Amines with p-Nitrobenzoyl Chloride and Picryl Chloride

R–C$_6$H$_4$–NH$_2$ R=	Electrophilic agent*	k_{25}° (liter/mole · sec)	k_{50}° (liter/mole · sec)	E_A (cal/mole)	lg A	ΔS# (cal/deg · mole)
C$_6$H$_5$–NH–	PC	2.98 ± 0.09	7.74 **	7300	5.83	—33.8
O$_2$N–C$_6$H$_4$–NH–	PC	0.0689 ± 0.0017	0.214 ± 0.004	8700	5.20	—36.8
C$_6$H$_5$–N=N–	PNBC	0.0121 ± 0.0003	0.0364 ± 0.0008	8400	4.27	—41.1
	PC	0.00214 ± 0.00005	0.00963 ± 0.00019	11500	5.77	—34.2
O$_2$N–C$_6$H$_4$–N=N–	PNBC	0.00231 ± 0.00009	0.00692 ± 0.00016	8400	3.52	—44.5
	PC	0.000285***	0.00132 ± 0.00006	11700	5.06	—37.6
C$_6$H$_5$–O–	PNBC	1.23 ± 0.03	2.60 ± 0.11	5550	4.17	—41.5
O$_2$N–C$_6$H$_4$–O–	PNBC	0.102 ± 0.003	0.273 ± 0.006	7500	4.53	—39.9
C$_6$H$_5$–S–	PNBC	0.120 ± 0.006	0.300 ± 0.012	7000	4.23	—41.2
O$_2$N–C$_6$H$_4$–S–	PNBC	0.00504 ± 0.00018	0.0178 ± 0.0008	9700	4.80	—38.5
C$_6$H$_5$–CH=CH–	PNBC	0.280 ± 0.012	0.755 ± 0.012	7600	5.01	—37.7
	PC	0.0619 ± 0.0020	0.222 ± 0.007	9800	5.96	—33.3
O$_2$N–C$_6$H$_4$–CH=CH–	PNBC	0.0573 ± 0.0032	0.126 ± 0.005	6000	3.18	—46.0
	PC	0.0121 ± 0.0005	0.0428 ± 0.0009	9700	3.18	—36.9
C$_6$H$_5$–	PNBC	0.533 ± 0.010	1.11 ± 0.02	5600	3.85	—42.8
	PC	0.0744 ± 0.0021	0.235 ± 0.003	8800	5.32	—36.2
O$_2$N–C$_6$H$_4$–	PNBC	0.0505 ± 0.0011	0.118 ± 0.003	6500	3.46	—44.7
	PC	0.00548 ± 0.00018	0.00205 ± 0.0009	10000	5.15	—37.1
H–	PNBC	0.580 ± 0.018	—	—	—	—
	PC	0.120 ± 0.002	0.394 ± 0.005	9100	5.75	—34.3

* PNBC – p-nitrobenzoyl chloride; PC – picryl chloride.

** Constant calculated from the data for lower temperature.

*** Constant calculated from data for higher temperature.

the amine in benzene; therefore the kinetic measurements were carried out at 50° and 70°, and the required value for the rate constant for 25° was calculated by the Arrhenius equation. The reality of this value was confirmed by the fact that it agreed with the value of the constants determined experimentally for one time interval only (20 hour, yield 25.9%): $k_{calc} = 0.000285$, and $k_{exp} = 0.000286$ liter/mole·sec.

The numerical data for the reaction of the amino derivatives of diphenylamine and azobenzene are given in detail in tables 2-7, where the following designations are used: k_i and k are the respective average values for the rate constant, 1) for a given segment of time t_i on number of measurements n_i, and 2) for all Σn_i measurements. In these tables in the second column we give average values for the yield of the reaction for the measurements n_i. In Table 8 are given the chief results of the kinetic studies in the present work, and also of some reactions which we studied earlier.

DISCUSSION OF RESULTS•

Comparison of the reaction rates of aniline and 4-aminodiphenylamine shows that introduction of the group C_6H_5NH- in the para position of the molecule of aniline permits a considerable increase in the rate, which indicates the clearly evident electron donor properties of this group. The very low reactivity of 4-aminoazobenzene compared to aniline certainly depends on the fact that the $C_6H_5N=N$- group is a strong electron acceptor.

As already mentioned above we can judge the intensity of transmission of reaction of the substituent from one benzene ring to the other in molecular systems of type (III) by the ratio of rate constants for the reaction of mono and disubstituted derivatives (factor f). In Table 9 we give values of f from which we see•• that in the molecular system of diphenylamine the effect of the nitro group on the reactivity of the amino group is especially strong. It is much more clearly shown than in the biphenyl system, where the benzene rings are joined directly together. We have already found such an effect in studying the reactivity of analogous derivatives of diphenyl oxide and diphenyl sulfide [1-3]. Actually, the values of f for the last two molecular systems are also greater than in the case of the biphenyl system. Thus, the introduction of one bridge heteroatom between the benzene rings in the biphenyl molecular system along with the spatial separation of these rings leads not to a weakening, but to a strengthening of the transfer of the effect of the nitro group on the reactivity of the amino group; here the effect does not depend on the electron donor or electron acceptor properties of the heteroatom bridge. All this, as already mentioned earlier [1-3], certainly depends on the presence in the heteroatom of an unshared p-electron which assures a p, π conjugation of the form

As a result of such conjugation there should occur on the heteroatom an effective positive charge (δ +), which is confirmed by the experimental results: all the substituents of $O_2N-C_6H_4-\ddot{M}-$, where $\ddot{M}$ is a bridge heteroatom, have electron acceptor properties (see Table 8). If the benzene rings are joined by a single-membered bridge in the form of a methylene group which does not contain an unshared p-electron (the molecular system of diphenylmethane), then here we find the effect usual for such cases, which show a weakened transfer of the effect of the nitro group on the reactivity of the amino group (compared to the biphenyl molecular system). It seems to us that this particularly emphasizes the value of p, π conjugation in the transfer of reaction of the substituent in molecular systems with bridge heteroatoms.

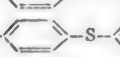
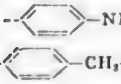
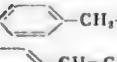
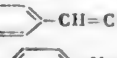
Although the bridge grouping -N=N- assures a single chain of conjugated double bonds between the opposite ends in a molecular system of azobenzene, the effect of the para substituent in this system is much weaker than in the case of a system with one bridge heteroatom (-O-, -S-, -NH-). This can be explained by the considerable spatial extent of the azobenzene molecular system, which contains a two-membered bridge, and again by the great

• See Table 8.

•• These values are of just the same type in qualitative and quantitative respects for both series of reactions. Only in reactions with picryl chloride f always is somewhat higher, which agrees with the special sensitivity of this reaction to structural changes in the molecules of the amino derivatives [15].

TABLE 9

Values of Factor f for Different Molecular Systems

Molecular systems	$f_{25°}$ for reaction with	
	p-nitrobenzoyl chloride	picryl chloride
[4]	10.6	13.6
[1, 3]	12.1	—
 [2, 3]	23.8	—
	—	43.3
 [6]	4.34	5.96
 [4]	4.89	5.12
	5.24	7.51

role of the p, π conjugation in the system with the one bridge heteroatom. The value of the factor f for the azobenzene molecular system is almost the same as in the case of the completely similar system of trans-stilbene [4], although both of the studied azobenzene derivatives were considerably less reactive than the analogous stilbene derivatives. The small increase in f on going from the stilbene system to the azobenzene system need scarcely be taken into account, although, possibly, it is also determined by the fact that in azobenzene transfer of the electron effect of the substituent, as assumed by V. A. Izmail'skii and E. A. Smirnov [17], occurs not only because of the π-electrons of the double bond in the azo group, but also partly from the unshared p-electrons of the nitrogen atom.

We have repeatedly observed previously [1-4, 6] that conclusions as to the reactions of substituents in such two-ring molecular systems with bridge atoms and groups, based on results of a chemical method of study, often differ from the results of spectroscopic study of such systems. The facts brought out in the present work further illustrate this position. Thus, according to the results of V. A. Izmail'skii and A. M. Simonov [18] the group -NH- in the diphenylamine molecular system plays the part of an insulator of the effect of conjugation and transfers only the inductive effect. The well-known book of Brode [19] states that this group is an insulator for optical effects, although it should be noted that on the basis of the same optical measurements (absorption spectra) A. A. Kharkharov [20] stated that in some conjugated systems replacement of the group -N=N- by the -NH- chain does not break the conjugation.

The relatively energetic parameters of the reactions studied in the present work can show that it proceeds at low values of E_A and $\Delta S^{\#}$, and somewhat higher values of these are characteristic of the reaction with the participation of picryl chloride than in the case of p-nitro benzoyl chloride. It should also be noted that for the reaction of different amines with the same electrophilic reagent when going from one amino derivative to another there occurs, in general, less change in $\Delta S^{\#}$ than in E_A. It is also important to consider that in the case of the reactions discussed in the present work on amino derivatives which have very long and complex molecules there is a marked effect on the temperature course of the rate constants from the presence in them of different degrees of hindrance to internal rotation around the single bond which joins one part of the molecule to the other (see [7]); this complicates treatment of the results from the point of view of change in value of E_A and $\Delta S^{\#}$ under the influence of structural factors. In view of all this, and considering that of the two experimentally available kinetic parameters it is the rate constant of the reaction and not the energy of activation (according to Arrhenius) that is the better value for judging the effect of consecutive structural changes in the molecule on the reactivity of the same functional group [21-23] (here we speak first of the transfer of the electron effect of the substituent on the functional group); in view of all this, we here, as in the previous papers in this series, continue to express the preference for measurement of the rate constant, guided by the above point of view.

SUMMARY

1. We have studied the kinetics of the reaction of 4-aminodiphenylamine, trans-4-aminoazobenzene, and their 4'-nitro derivatives with p-nitrobenzoyl chloride and picryl chloride in benzene solution.

2. Comparing the results of our work with the kinetic characteristics of the earlier studied analogous reactions shows that the 4'-NO_2 group in the diphenylamine molecular system, in which the benzene rings are joined to each other by a heteroatom bridge, affects the reactivity of the 4-NH_2 group considerably more strongly than in the biphenyl system, where the benzene rings are joined directly to each other, which indicates the great intensity in transfer of the electron effects of the substituent (from one benzene ring to the other) in the first of the above-mentioned systems. In the transfer of these effects in the diphenylamine system a considerable role is played by the p, π conjugation of the unshared p electron of the heteroatom bridge with the π electrons of the benzene ring.

3. In the azobenzene molecular system the effect of the 4'-NO_2 group on the reactivity of the 4-NH_2 group is weakly shown, due to the considerable spatial distance of the groups from each other compared to the biphenyl system. Although the bridging molecular grouping -N=N- in the azobenzene system contains easily mobile π electrons, it is a much poorer conductor of electron effects than the analogous bridging link -NH- in the diphenylamine system, where there is a clearly shown effect of p, π conjugation.

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STUDIES IN THE NAPHTHALENE SERIES

XIX. 1,3,7-TRIHYDROXYNAPHTHALENE*

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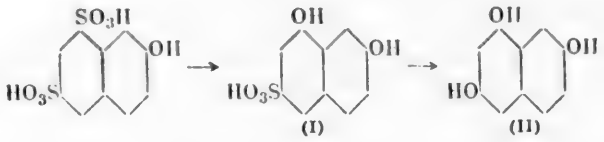
In order to widen our ideas on the possibility of successfully carrying out alkaline fusion of meta-substituted disulfonic and hydroxysulfonic derivatives of naphthalene to give dihydroxy derivatives [1, 2] we have studied the relation to alkaline fusion of naphthalene 2-hydroxy-6,8-disulfonic acid (G acid).

Some indications confirm the possibility of transformation of polysubstituted naphthalenes without splitting the naphthalene ring. Thus, it is possible in alkaline fusion of 1-hydroxynaphthalene-3,6,8-trisulfonic acid to transform it into 1,8-dihydroxynaphthalene-3,6-disulfonic acid [3], and then to 1,3,8-trihydroxynaphthalene-6-sulfonic acid [4]; transformation occurs of 2-hydroxynaphthalene-6,8-disulfonic acid into 2,8-dihydroxynaphthalene-6-sulfonic acid [5]. There is also evidence that alkaline fusion of G acid itself [6] and of 2,8-dihydroxynaphthalene-6-sulfonic acid [7] leads to formation of hydroxytoluic acid.

We were interested in the possibility of carrying out the final conversion of 2-hydroxynaphthalene-6,8-disulfonic acid in accordance with the scheme



Of the possible isomers of trihydroxynaphthalene which have two hydroxy groups in the meta position, only 1,3,6-trihydroxynaphthalene has been described in detail; it is obtained by alkaline fusion of 1,6-dihydroxynaphthalene-3-sulfonic acid [8].

The technical K salt of 2-hydroxynaphthalene-6,8-disulfonic acid (83.8%) or its recrystallized form (94%) was added to fused potassium hydroxide in an open copper vessel heated by a metal bath with the flame of a burner and stirred by hand in a copper casing with a thermometer or in a copper vessel with an electric heater and a mechanical stirrer. The fusion was dissolved in water, neutralized to a strongly acid reaction, filtered from tars, and in the solution was determined the content of reaction products and also the remaining unchanged G salt. The yields of products of the fusion depending on temperature and time are given in Tables 1 and 2. These tables show that the optimum conditions for converting 2-hydroxynaphthalene-6,8-disulfonic acid are: to 2,8-dihydroxynaphthalene-6-sulfonic acid (I) 200-205°, and to 1,3,7-trihydroxynaphthalene (II), 260-265° in the course of one hour. Lowering the temperature of the melt to 180° raises the amount of unchanged 2-hydroxynaphthalene-6,8-disulfonic acid, and raising the temperature to 270° lowers the yield of trihydroxynaphthalene due to formation

* Communication XVIII, see Zhur. Obshchei Khim. 28, 3333 (1958).

TABLE 1

Alkaline Fusion of G Salt. Effect of Temperature (5.0 g of 83.8% K salt of 2-hydroxynaphthalene-6,8-disulfonic acid; 10 g KOH; 3.0 ml H_2O; 1 hour)

No.	Temperature	Obtained (%) trihydroxynaphthalene	dihydroxy-G acid	unchanged G salt
1	180—185°	—	69.3	31.2
2	200—205	4.3	76.0	18.1
3	220—225	13.9	51.5	35.4
4	240—245	37.4	52.0	10.3
5	260—265	65.7	12.0	—
6	270—275	54.0	Trace	—

TABLE 2

Alkaline Fusion of G Salt. Effect of Time (5.0 g of 83.8% K salt of 2-hydroxynaphthalene-6,8-disulfonic acid; 10 g KOH; 3 ml H_2O)

No.	Temperature	Time (in minutes)	Obtained (in %) trihydroxynaphthalene	dihydroxy-G acid	unchanged G salt
1	200—205°	60	4.3	76.0	18.1
2		90	1.9	29.7	—
3	240—245	60	37.4	52.0	10.3
4		90	12.3	Trace	—
5	260—265	15	18.0	50.5	24.6
6		30	44.7	29.2	12.0
7		40	52.7	11.4	—
8		60	65.7	12.0	—

of products from opening the naphthalene ring. Increasing the time of reaction above one hour has the same effect. Melts with various amounts of potassium hydroxide and with sodium hydroxide (Table 3) show that formation of hydroxy derivatives of naphthalene occurs best by melting with potassium hydroxide in a ratio of it to the starting G salt of 2.4-2.5:1. A favorable course of the fusion process follows from purity of the starting G salt which is best used dry, and still better, in the form of a naphtholate salt first prepared and dried. All these conditions lower the possibility of oxidative-hydrolytic transformations as a result of which 1, 3,7-trihydroxynaphthalene can be split at carbon to carbon bonds.

Autoclaving a melt of G salt with a 43% solution of potassium hydroxide at 200° for one hour limits the reaction only to the formation of 2,8-dihydroxynaphthalene-6-sulfonic acid (up to 70%) with traces of the trihydroxy compound. The amount of unfused salt corresponds to about 10%. Addition of hydrosulfite to the open melt leads to a decreased yield with half as much trihydroxynaphthalene, but the product contains almost no tar and is easily purified by crystallization. For separation of trihydroxynaphthalene, the acid solution obtained by neutralizing the alkaline fusion was extracted with ether. The substance was crystallized from water in light sandy-colored plates with m.p. 152°. It was very hygroscopic and even though dried over P_2O_5 it retained one or two molecules of water. Its water solution gave a red-violet color, which disappeared on standing, with a drop of ferric chloride, and with a drop of bleaching powder solution it gave a light-red color. The substance dissolved very easily in ether, solutions of soda and bisulfite, in methyl and ethyl alcohols, and acetone, was difficultly soluble in benzene, and did not dissolve in chloroform and ligroin. On long standing in air the solution of trihydroxynaphthalene gradually darkened and a product separated which was difficultly soluble in water, did not melt, and was gradually converted into a tar.

1,3,7-Trihydroxynaphthalene forms by coupling with diazonium compounds in soda solution only a monoazo dye, does not form a nitroso compound, is difficult to convert to 1,3,7-trichloronaphthalene, very difficult to acetylate with acetic anhydride, forming a triacetoxynaphthalene only with acetyl chloride. In the reaction of a water solution of trihydroxynaphthalene with acetic or hydrochloric acid there is formed a dark-brown precipitate insoluble in water and nonmelting (dimer). All these properties of trihydroxynaphthalene permit us to suggest the possibility of its existence in a keto form

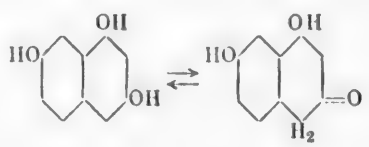


TABLE 3

Alkaline Fusion of G Salt. Effect of Nature of the Alkali (5.0 g of 83.8% K salt of 2-hydroxynaphthalene-6,8-disulfonic acid; 0.18 g-mole KOH or NaOH, 3 ml of H_2O; 1 hour)

No.	Alkali	Temperature	Obtained (in %)		
			trihydroxynaphthalene	dihydroxy-G acid	unchanged G salt
1	KOH	200—205°	4.3	76.0	18.1
2	NaOH	200—205°	—	31.0	57.0
3	KOH	260—265	65.7	12.0	—
4	NaOH	260—265	49.0	15.0	—

The properties of this trihydroxynaphthalene are very similar to those of 1,3,6-trihydroxynaphthalene [8] whose structure shows two tautomeric forms. Our 1,3,7-trihydroxynaphthalene is an interesting oxidizing pigment for fur.

EXPERIMENTAL

Fusion of the K salt of 2-hydroxynaphthalene-6,8-disulfonic acid (G salt) with alkalis. In a 200 ml copper vessel we melted 12.6 g of potassium hydroxide (80.3%) with 3 ml of water at a given temperature. With energetic hand stirring with a copper casing containing a thermometer we gradually added 5 g of dry (83.8%) G salt. The melt was kept for a determined period, then transferred to a porcelain beaker or dish where it was dissolved in 150 ml of water and neutralized with concentrated sulfuric acid to a strongly acid reaction to Congo.

When the sulfonate was added to the fused alkali in small portions foaming did not occur. At first the melt was thick but mobile, dark-yellow in color; it gradually thickened and at the end was dry and orange brown. After neutralization of the solution it was kept for 12 hours, separated from the tar, and boiled with a small amount of animal charcoal to complete removal of sulfur dioxide. The resulting solution was placed in a calibrated flask for analysis. The analysis of the contents of the solution was carried out by titration with a solution of diazo-m-nitroaniline successively in soda and acetic acid solutions.

The starting G salt (2-hydroxynaphthalene-6,8-disulfonic acid), the intermediate product of the fusion, 2,8-dihydroxynaphthalene-6-sulfonic acid, and the final product of the fusion, 1,3,7-trihydroxynaphthalene coupled well with diazo-m-nitroaniline in soda solution. Besides this, as we showed, 2-hydroxynaphthalene-6,8-disulfonic acid (G salt), in distinction from 2,8-dihydroxynaphthalene-6-sulfonic acid, does not couple with the same diazo compound in acetic acid. In all cases the monoazo dye was formed.

A combined sample of solution of the melt in soda solution determined the sum of the naphthalene sulfonic acids (2-hydroxynaphthalene-6,8-disulfonic acid and 2,8-dihydroxynaphthalene-6-sulfonic acid) and trihydroxynaphthalene. Such a combined sample, but after extraction of the trihydroxynaphthalene by ether in a soda solution, gave the sum of the above-mentioned naphthalene sulfonic acids. The difference in results of the titration of the first and second samples gave the amount of trihydroxynaphthalene.

A parallel second sample of the solution (without trihydroxynaphthalene) in acetic acid determined the amount of 2,8-dihydroxynaphthalene-6-sulfonic acid. The difference in results in soda and acetic acid solutions allowed us to determine the amount of 2-hydroxynaphthalene-6,8-disulfonic acid (G salt) unchanged in the fusion. In the solution from the fusion of the G salt we established qualitatively the presence of salts of acetic, o-toluic, and hydroxytoluic acids.

Analysis of 1,3,7-trihydroxynaphthalene and its derivatives. The crude product isolated from the ether extract had a dark-brown color and a m.p. 98-100°. After recrystallization from water and drying over P_2O_5, m.p. 152°.

Found %: H_2O 10.58. $C_{10}H_8O_3 \cdot H_2O$. Calculated %: H_2O 9.3.
Found %: H_2O 17.6. $C_{10}H_8O_3 \cdot 2H_2O$. Calculated %: H_2O 16.98.
Found %: C 67.74, 67.71; H 4.54, 4.70. $C_{10}H_8O_3$. Calculated %: C 68.1; H 4.54.

Preparation of the acetyl derivative. We heated 0.3 g of 1,3,7-trihydroxynaphthalene, 2.5 g of acetyl chloride, and 3 drops of pyridine for 6 hours at 35-37° in a round-bottomed flask with a reflux condenser. When the reaction mass was poured over ice it gave an oily product with a dark-brown color which after washing with water was dried in a desiccator over P_2O_5 to a solid mass. The yield of triacetoxynaphthalene was 20%. The substance was easily soluble in acetic acid and alcohol. It crystallized from dilute acetic acid in fine, light-gray crystals with m.p. 205°.

Saponification of the substance for four hours by heating to boiling with a solution of 0.5 N alcoholic KOH and later potentiometric titration by 0.1 N HCl to pH 8.2 led to formation of the naphtholate.

Found: acetyl number 1284. $C_{10}H_4(OCOCH_3)_3$. Calculated: acetyl number 1114.5.

Preparation of 1,3,7-trichloronaphthalene from trihydroxynaphthalene. We moistened 0.3 g of trihydroxynaphthalene with 2 drops of phosphorus oxychloride, mixed it with 1.2 g of PCl_5 and heated under reflux in a round-bottomed flask on an oil bath for six hours at 180°. The resulting chloronaphthalene melted at 113° and showed no depression in a mixed sample with pure 1,3,7-trichloronaphthalene.

Formation of an azo dye from trihydroxynaphthalene. In coupling 1,3,7-trihydroxynaphthalene with diazo-m-nitroaniline in a soda solution we formed a mono azo dye with a red color which crystallized from water.

Found %: H_2O 9.5 . Tin number 110.9. $C_{10}H_{11}O_5N_3 \cdot 2H_2O$. Calculated %: H_2O 10.0, tin number 110.8.

Quantitative titration of 0.3020 g of trihydroxynaphthalene in soda solution (31 ml of 0.05 N diazo-m-nitroaniline solution) also showed the formation of a monoazo dye and a content in the substance of 99.57% ($C_{10}H_8O_3 \cdot 2H_2O$).

Characteristics of the K salt of 2,8-dihydroxynaphthalene-6-sulfonic acid. It was crystallized from a 15% solution of sodium chloride in long, light prisms. Easily soluble in water, methyl, and ethyl alcohols. The water solution of the salt gives a quickly disappearing green-yellow color with a solution of ferric chloride, and with a solution of bleaching powder, a red color which is characteristic for this substance [5].

Found %: H_2O 11.6. $C_{10}H_7O_5SK \cdot 2H_2O$. Calculated %: H_2O 11.4. Found %: K 13.42. $C_{10}H_7O_5SK$. Calculated %: K 14.02.

In coupling the substance in acetic acid with diazo-m-nitroaniline there is formed a bright-red dye, difficultly soluble in cold water.

Found: tin number 89.1. $C_{10}H_{10}O_7N_3SK$. Calculated: tin number 93.8.

SUMMARY

1. We have synthesized 1,3,7-trihydroxynaphthalene by alkaline fusion of 2-hydroxynaphthalene-6,8-disulfonic acid (G salt).

2. The properties of the substance, its color, easy solubility in bisulfite solution, formation by coupling with diazonium compounds of only a monoazo dye, difficulty of acetylation, ability to retain water and to darken from acetic and hydrochloric acids, inability to form a nitroso compound, all permit us to assume for this new trihydroxynaphthalene the structure of a hydroxyketone.

3. The substance is recommended as an oxidizing dye for fur.

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THE ACYLATION OF MONOACYLATED HOMOLOGS OF THIOPHENE

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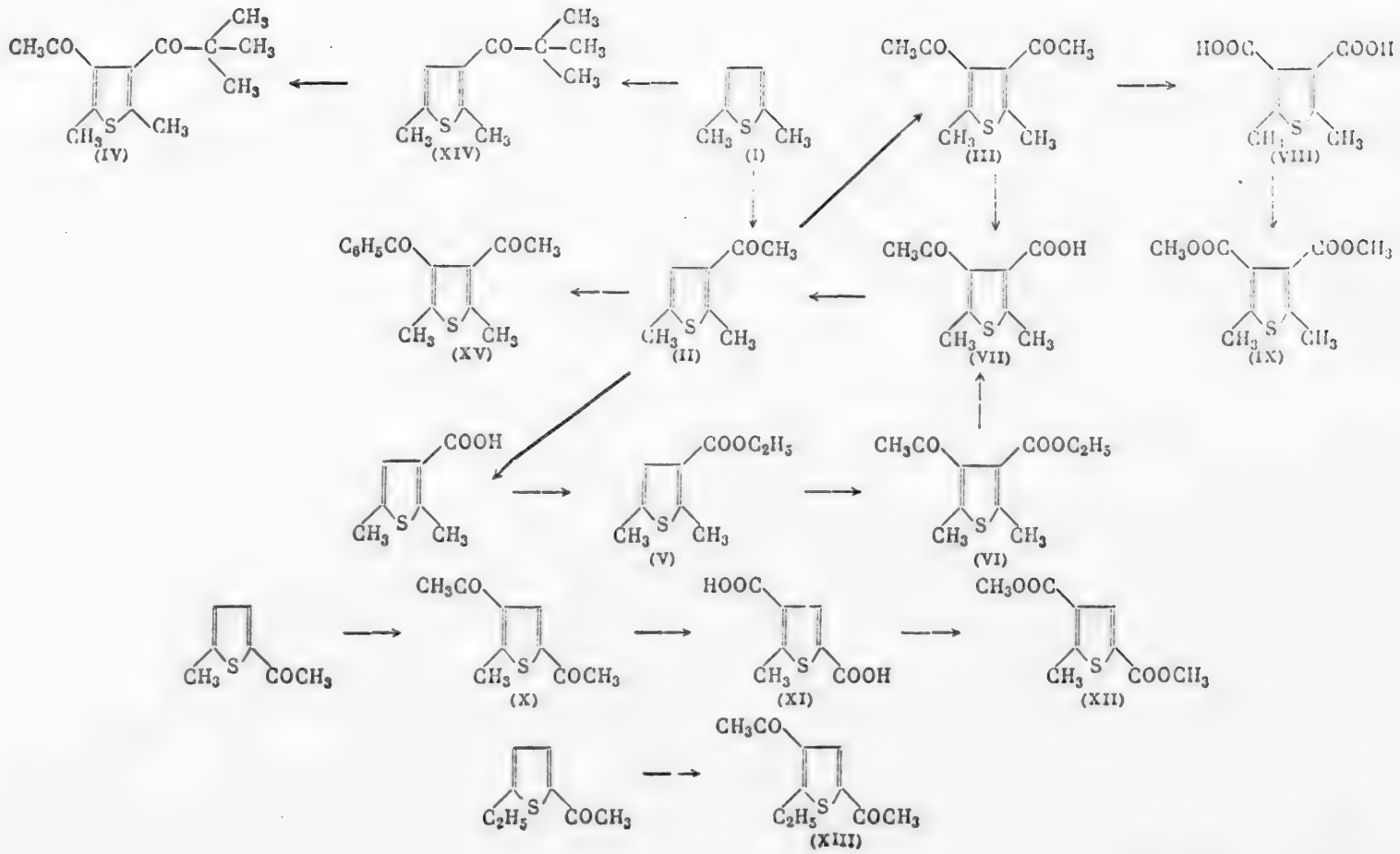
Previously we and V. I. Shvedov [1] showed that β-atoms of hydrogen in 2,5-dialkylated thiophenes are more easily replaced by acyl residues than α-atoms of hydrogen in unsubstituted thiophenes, which are known to be distinguished by their great mobility. The reason for such a change in reactivity lies in the induction effect of the alkyl group or is connected with a hyperconjugation effect. However, what would be the mechanism of action in an aromatic (thiophene) ring substituent of a similar type depends in the last analysis on the increase in electron density of the ring*, which is shown by increasing reactivity with respect to electrophilic agents. This is evidently the reason why 2,5-dimethyl thiophene (I) easily forms a 3,4-dinitro derivative [3] and 3,4-disulfonic acid [4] (in the form of an inner anhydride). In view of these results it seems there is full likelihood of formation of a 3,4-diacylated homolog of thiophene by direct acylation, which would be of interest to us in connection with our work on the synthesis of bifunctional derivatives of the thiophene series [5]. We have found in this connection that even in 1886 Schweinitz [6] obtained by acetylation of octyl thiophene in the presence of aluminum chloride both monoacetyl and diacetyl derivatives of octylthiophene. Recently Hartough and Kosak [7] described 2,5-diacetylthiophene, which they synthesized, with a yield of only 6%, by the action of acetic anhydride on 2-acetothienone in the presence of zinc chloride, and then 2,5-dipropanoylthiophene [8] and 2,5-didecanoylthiophene [9], formed with a yield of 23% along with 2-decanoylthiophene by heating thiophene with the corresponding acid in the presence of phosphorus pentoxide. A different relation is found in the benzene series: benzene, toluene, o-xylene and p-xylene, as Meyer and Pavia [10] found, under the conditions of the Friedel-Crafts reaction do not give diacetyl derivatives. On the other hand, mesitylene, durene, and isodurene, which include the structural grouping held by Meyer to be required for diacetylation, a meta-orienting methyl group, easily form the corresponding diketone in the presence of excess aluminum chloride [11]. The findings of the authors [10] relative to pseudocumene and m-xylene agree with this viewpoint, but it was shown much more recently [12] that direct acylation can give good yields of 2,4-diacetyl-m-xylene and small yields of 3,5-diacetylpseudocumene. By comparing these results we can again confirm the conclusion that the idea of the analogy between benzene and thiophene which for a long time has served as the directing principle in the study of thiophene chemistry has only a very limited value [13]. This is also confirmed by the results of our study of the acylation of 2,5-dimethylthiophene (I). The monoacyl derivative of this compound, 2,5-dimethyl-3-acetothienone (II), as we had assumed, under the action of acetyl chloride in the presence of aluminum chloride in dichloroethane (Process A) forms a compound with the composition $C_{10}H_{12}O_2S$, whose structure as 2,5-dimethyl-3,4-diacetylthiophene (III) is undoubted (see below).

The yield of (III) can be raised several fold, to 87%, by carrying out the acetylation in the presence of a great excess of aluminum chloride and without a solvent (Process B) corresponding to the description for getting

*Recently the question of the nature of the action of alkyl substituents in an aromatic ring has again been discussed, and in particular Pearson [2] considers that the question of the nature of action of substituents in an aromatic ring has produced inconsequential results.


(IV)
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(XIII)

diacetyl-m-xylene [14]. The reason for such a marked rise in yield under these conditions is not entirely clear, since the formation of a complex of the starting monoketone with aluminum chloride, like that assumed by Pearson and Pope [15] for acetophenone, would required lowering of the electron density of the ring and should result in lowering of the reaction rate with electrophilic reagents. On the other hand, the absence of a solvent, which often forms an addition product with the catalyst and therefore inhibits the activity of the latter in the Friedel-Crafts reaction, [15], should actually have a positive effect on the process [16]. It is a very interesting fact that under comparable conditions 2,5-dimethyl-3-pivalylthiophene is acetylated with the same yield though it contains a sterically large residue of trimethyl acetic acid; it is possible that in this case the fact is important that the angle formed by the substituent in position 3 [17] with the ring greatly surpasses that in benzene. Since in acetylation of 2,5-dimethyl-3-pivalylthiophene there is no possibility of the attack of the acyl residue on acetylation, as is sometimes found when BF_3 is used as the catalyst [18], the structure of the resulting diketone as 2,5-dimethyl-3-acetyl-4-pivalylthiophene (IV) is certain. For analogous reasons we can consider established the structure of the product of acetylation (VI) of the ethyl ester of 2,5-dimethyl-3-thiophene carboxylic acid (V), which is formed in a yield of about 55% when acetyl chloride acts on the latter under the conditions of process B. Attempts at benzoylation of 2,5-dimethyl-3-acetothienone (II) under the same conditions lead only to a slight yield of diketone (XV). It is possible that under these conditions the process goes preferentially to dislodging the acetyl group by the benzoyl; these experiments require further study. We note here that in attempts to obtain the diketone (IV) by the action of acetyl iodide on 2,5-dimethyl-3-pivalylthiophene in the absence of aluminum chloride there is formation of trimethyl acetic acid.

The structures of the products of acetylation of the monoketone (II) and the diketone (III) were established as follows. By oxidation of the diketone (III) with sodium hypochlorite we obtained a ketoacid whose structure as 2,5-dimethyl-4-acetyl-3-thiophenecarboxylic acid (VII) follows from the fact that in its properties it agrees with the acid obtained from saponification of ester (VI). In turn, the structure of acid (VII) is confirmed by the formation from it in its decarboxylation of 2,5-dimethyl-3-acetothienone (II). Finally, it remains to mention that the formation in the oxidation of (III) of the dicarboxylic acid (VIII) and from the latter the diester (IX) also agrees with the assumed structure of (III) which is formed by the action of acetyl chloride on 2,5-dimethyl-3-acetothienone (II).

These results again confirm the opinion of Steinkopf [19] that the 3,4-positions of thiophene cannot be compared with the ortho or para positions of benzene. The orienting effect of substituents in the 3 and 4 positions of thiophene rings is not the same as that which has been worked out in developing the chemistry of benzene.

Process B, which permits a considerable increase in yield of 3,4-diacyl derivatives, is also useful in the synthesis of 2,4-diacyl compounds of the thiophene series. Thus the 2,4-diketones can be obtained in yields on the order of 60%, while in work with solvents the yields are very small. By hypochlorite oxidation of the 2-methyl-3,5-diacetylthiophene (X) which we obtained we formed the corresponding dicarboxylic acid and by the action of diazomethane we obtained the diester (XII).

In the light of these results it is interesting that attempts to obtain a diketone from unsubstituted thiophene by process B were not successful; we recovered about 80% of the starting 2-acetothienone. Thus we must have the simultaneous presence of alkyl groups and acetyl radicals in order to introduce a second acyl residue into the thiophene ring. This is still more noteworthy since in the case of an unsubstituted 2-acetothienone, position 4, which corresponds to the meta position of the benzene ring, while at first glance less favorably situated, by the action of acylating agents on 2,5-dimethyl-3-acetothienone, is actually acetylated in good yield. We note in this connection that according to Imoto and co-workers [20] the 2,5-positions of thiophene are like the para positions of benzene.

EXPERIMENTAL

2,5-Dimethyl-3,4-diacetylthiophene (III). A) To a solution of 7.7 g of 2,5-dimethyl-3-acetothienone in 40 ml of dichloroethane was added 4.7 g of acetyl chloride. Then, with strong stirring, over 30 minutes in small portions 13.3 g of aluminum chloride was added. The mixture was heated for 3.5 hours at 90°, then cooled to 10° and decomposed with dilute hydrochloric acid (5 ml of concentrated acid and 45 ml of water). The water layer was separated from the dichloroethane and extracted with 70 ml of dichloroethane. The dichloroethane layer was washed with water, 1% sodium hydroxide solution, and was combined with the dichloroethane extract and dried with calcium chloride. The solvent was distilled off and the residue distilled in a vacuum. We collected the fractions:

1st. B.p. 110-112° (13 mm), 4.5 g, nD^{20} 1.5459, starting 2,5-dimethyl-3-acetothienone; literature gives b.p. 62° (0.25 mm), nD^{20} 1.5452; 2nd, B.p. 195-196° (13 mm), crystallizing in the refrigerator. After recrystallization from water we obtained white glittering crystals with m.p. 88-89°, easily soluble in ether, ethyl acetate, and alcohol. Yield 13.2% based on taken and 32.2% based on reacting 2,5-dimethyl-3-acetothienone.

Found %: C 61.39, 61.40; H 6.25, 6.17; S 16.31, 16.33. $C_{10}H_{12}O_2S$. Calculated %: C 61.19; N 6.16; S 16.33.

B) To 13.9 g of anhydrous aluminum chloride with stirring during 15 minutes we added dropwise 6.5 g of 2,5-dimethyl-3-thienone. To the warm liquid complex during 20 minutes we added dropwise 4.8 g of acetyl chloride and stirred the mixture at room temperature for 3 hours. The solidified reaction mass was transferred in pieces to a flask with ice and 20 ml of concentrated hydrochloric acid. The resulting yellow precipitate was filtered and washed with water. We obtained 7.15 g (87.3%), m.p. 88-89° (from water).

Found %: C 61.00, 60.78; H 6.12, 6.11; S 16.23, 16.11. $C_{10}H_{12}O_2S$. Calculated %: C 61.19; H 6.16; S 16.33.

Dioxime, m.p. 164.5-165° (from aqueous alcohol).

Found %: N 12.73, 12.51. $C_{10}H_{14}O_2N_2S$. Calculated %: N 12.38.

2,5-Dimethyl-3-pivalylthiophene (XIV). To a solution of 22.4 g of 2,5-dimethylthiophene in 120 ml of chlorobenzene was added 28 g of pivalic acid chloride. After stirring for 40 minutes at minus 3-5° we added dropwise 30.8 g of tin chloride in 30 ml of chlorobenzene. The mixture was stirred at room temperature for three hours, then treated as in the preparation of 2,5-dimethyl-3,4-diacetylthiophene (Process A). After distillation of the solvent the residue was distilled in a vacuum. We collected the fractions:

1st, b.p. 96-97° (5 mm), 2.0 g, nD^{20} 1.5210; 2nd, b.p. 97-99° (5 mm), 15.3 g, nD^{20} 1.5191. Residue, tar, 2.3 g.

Found %: C 67.38, 67.40; H 8.27, 8.11; S 16.10, 16.24. $C_{11}H_{16}OS$. Calculated %: C 67.30; H 8.21; S 16.37.

2,5-Dimethyl-3-acetyl-4-pivalylthiophene (IV). This was synthesized under conditions analogous to those for preparing 2,5-dimethyl-3,4-diacetylthiophene (Process A) from 7 g of 2,5-dimethyl-3-pivalylthiophene and 3.4 g of acetyl chloride in 28.5 ml of dichloroethane with the aid of 9.6 g of aluminum chloride. After vacuum distillation we collected the fractions: 1st, b.p. 76-100° (5 mm), 3.5 g, nD^{20} 1.5231; 2nd, b.p. 100-152° (5 mm), 1.13 g, which crystallized in the refrigerator. After recrystallization from water we obtained white needle-like crystals with m.p. 66-67°.

Found %: C 65.79, 65.40; H 7.58, 7.47; S 13.02, 13.19. $C_{13}H_{18}O_2S$. Calculated %: C 65.51; H 7.60; S 13.45.

2,5-Dimethyl-3-acetyl-4-benzoylthiophene (XV). This was synthesized using the somewhat changed conditions for getting 2,5-dimethyl-3,4-diacetylthiophene (Process B) from 6.16 g of 2,5-dimethyl-3-acetothienone, 8.15 g of benzoyl chloride, and 13.3 g of aluminum chloride. After addition of the benzoyl chloride the mixture was heated for 10 minutes at 60°, stirred at room temperature for one hour, and allowed to stand for 36 hours at room temperature. The hardened reaction mass was transferred in pieces to a flask with ice and 20 ml of concentrated hydrochloric acid. The yellow oil which precipitated was extracted with ether. The extract was washed with a saturated solution of sodium bicarbonate and with water, and was dried over calcium chloride. After distillation of the solvent, the residue was vacuum distilled. We obtained the following fractions: 1st, b.p. 62-82° (4 mm) 3.9 g, nD^{20} 1.5495; 2nd, b.p. 82-102° (4 mm), 2.4 g, nD^{20} 1.5471; 3rd, b.p. 102-188° (4 mm), 0.14 g, nD^{20} 1.5491. These fractions were not studied but evidently they are chiefly the starting 2,5-dimethyl-3-benzoylthiophene. At the end of the distillation a little substance crystallized in the refrigerator; after recrystallization from water we obtained 0.03 g of white crystals with m.p. 90-91°, evidently 2,5-dimethyl-3-acetyl-4-benzoylthiophene.

Found %: C 69.35, 68.58; H 5.57, 5.37; S 12.01, 11.86. $C_{15}H_{14}O_2S$. Calculated %: C 69.73; H 5.46; S 12.41.

Ethyl 2,5-dimethyl-3-thiophenecarboxylate (V). A solution of 20.4 g of 2,5-dimethyl-3-thiophenecarboxylic acid in 84 ml of anhydrous alcohol saturated with hydrochloric acid was heated for three hours on a water bath and then washed with water. The lower layer was separated, the upper was extracted with ether. The combined lower layer and ether extract were washed with a saturated solution of sodium bicarbonate, with water, and were dried with magnesium sulfate. After distillation of the ether, the residue was vacuum distilled; we obtained 20.6 g (86%) with b.p. 98-99° (5 mm), nD^{20} 1.5161.

Found %: C 58.77, 58.58; H 6.75, 6.55; S 17.02, 17.09. $C_9H_{12}O_2S$. Calculated %: C 58.66; H 6.56; S 17.40.

Ethyl 2,5-dimethyl-4-acetyl-3-thiophenecarboxylate (VI). This was synthesized under conditions for getting 2,5-dimethyl-3,4-diacetylthiophene (Process B) with slight changes. To 21.3 g of aluminum chloride was added dropwise with stirring 22.1 g of acetyl chloride. To the warm liquid complex we added dropwise 11.9 g of ethyl 2,5-dimethyl-3-thiophenecarboxylate. The mixture was stirred for six hours at room temperature and left over night. The solidified reaction mass was treated as described above. After vacuum distillation we obtained the following fractions: 1st, b.p. 100-122° (4 mm), 3.02 g, nD^{20} 1.5173; 2nd, b.p. 122-130° (4 mm), 0.60 g, nD^{20} 1.5209; 3rd, b.p. 130-132° (4 mm), 7.9 g (54.6%), nD^{20} 1.5242. After repeated distillations the 3rd fraction had b.p. 130-132° (4 mm).

Found %: C 58.16, 58.30; H 6.12, 6.17; S 14.31, 14.40. $C_{11}H_{14}O_3S$. Calculated %: C 58.37; H 6.23; S 14.16.

We saponified 7.2 g of ethyl 2,5-dimethyl-3-acetyl-4-thiocarboxylate by heating it for 2.5 hours with 12.7 g of sodium hydroxide in 50 ml of water. We obtained 6.2 g (98.4%) of 2,5-dimethyl-4-acetyl-3-thiophenecarboxylic acid with m.p. 155-156° (from aqueous alcohol). A mixed sample with 2,5-dimethyl-4-acetyl-3-thiophenecarboxylic acid obtained by oxidation of (III) gave no depression.

2,5-Dimethyl-4-acetyl-3-thiophenecarboxylic acid (VII) was synthesized by the method described in the literature for obtaining 5-acetyl-2-thiophenecarboxylic acid [7] with sodium hypochlorite. From 1.04 g of 2,5-dimethyl-3,4-diacetylthiophene we obtained 0.12 g of needle-like crystals with m.p. 155-156° (from water).

Found %: C 54.30, 54.14; H 5.09, 5.29; S 15.90, 15.83. $C_9H_{10}O_3S$. Calculated %: C 54.53; H 5.08; S 16.17.

A mixed sample with acid obtained by saponifying ethyl 2,5-dimethyl-4-acetyl-3-thiophenecarboxylate gave no melting point depression. Three g of the resulting 2,5-dimethyl-4-acetyl-3-carboxylic acid were heated with 20 ml of distilled quinoline in the presence of about 5 mg of copper powder at 240° in a bath. During 1.5 hours there evolved 320 ml of carbon dioxide (theoretical amount 345 ml); the mixture was poured into 100 ml of water, acidified with hydrochloric acid to an acid reaction to Congo, and extracted with ether; the extract was washed with water, with a saturated bicarbonate solution, and was dried with calcium chloride. After distillation of the solvent, the residue was distilled in a vacuum. We obtained 1.25 g (51.3%) of 2,5-dimethyl-3-acetothienone with b.p. 124-126° (28 mm), nD^{20} 1.5479.

Found %: C 62.25, 62.55; H 6.58, 6.59; S 19.35, 19.61. $C_8H_{10}OS$. Calculated %: C 62.29; H 6.53. S 20.79.

Semicarbazone m.p. 211-212° (from alcohol).

Found %: N 19.42, 19.61. $C_9H_{13}ON_3S$. Calculated %: N 19.88.

A sample mixed with the semicarbazone of 2,5-dimethyl-3-acetylthiophene, obtained by acetylation of 2,5-dimethylthiophene, gave no melting point depression (m.p. 211-212°).

2,5-Dimethyl-3,4-thiophenedicarboxylic acid (VIII). Oxidation of 2,5-dimethyl-3,4-diacetylthiophene was carried out under the conditions described above with sodium hypochlorite. From 5.15 g of 2,5-dimethyl-3,4-diacetylthiophene we obtained 2.25 g of needle-like crystals with m.p. 201-202° (from water, in a sealed capillary).

Found %: C 47.54, 47.49; H 4.13, 3.98; S 15.54, 15.51. $C_8H_8O_4S$. Calculated %: C 47.99; H 4.02; S 16.01.

Dimethyl 2,5-dimethyl-3,4-thiophenedicarboxylate (IX). We dissolved 1.34 g of 2,5-dimethyl-3,4-thiophenecarboxylic acid in 175 ml of absolute ether (part of the acid did not dissolve) and over 30 minutes added dropwise 81 ml of an ether solution of diazomethane which contained about 1.96 g of diazomethane; the solution was filtered and the ether distilled off. We obtained 1.45 g (95.4%). M.p. 63-64° (from 50% alcohol).

Found %: C 52.65, 62.58; H 5.32, 5.53; S 13.92, 13.92. $C_{10}H_{12}O_4S$. Calculated %: C 52.61; H 5.30; S 14.04.

2-Methyl-3,5-diacetylthiophene (X) was obtained under conditions analogous to those for getting 2,5-dimethyl-3,4-diacetylthiophene (process B) from 13.4 g of 2-methyl-5-acetothienone and 9.12 g of acetyl chloride in the presence of 32 g of aluminum chloride. Yield 9.96 g (57%), m.p. 94-95°.

Found %: C 59.30, 59.48; H 5.71, 5.47; S 17.43, 17.51. $C_9H_{10}O_2S$. Calculated %: C 59.31; H 5.53; S 17.59.

2-Ethyl-3,5-diacetylthiophene (XIII) was obtained under the conditions described above with slight changes. A mixture of 7.7 g of 2-ethyl-5-acetothienone, 16.7 g of aluminum chloride, and 4.7 g of acetyl chloride was heated for three hours at 50-55° and the amorphous precipitate which settled out was extracted with ether; from the ether extract after washing and drying with calcium chloride and distillation of the solvent, vacuum distillation

of the residue gave the following fractions: 1st b.p. 126-140° (4 mm), 0.4 g, nD^{20} 1.5561; 2nd, b.p. 140-143.5° (4 mm), 5.9 g which crystallized. M.p. 47-48° (from aqueous alcohol). Yield 60%.

Found %: C 61.17, 61.34; H 6.26, 6.31; S 16.17, 16.32. $C_{10}H_{12}O_2S$. Calculated %: C 61.19; H 6.16; S 16.33.

5-Methyl-2,4-thiophenedicarboxylic acid (XI). Oxidation of 2-methyl-3,5-diacetylthiophene was carried out by the method described in the literature for oxidation of 2,5-diacetothienone [7]. From 6.7 g of 5-methyl-2,4-diacetylthiophene with sodium hypochlorite we obtained 5.6 g of 5-methyl-2,4-thiophenedicarboxylic acid with m.p. 278-279° (from water, in a sealed capillary).

Found %: C 45.47, 45.38; H 3.71, 3.57; S 16.95, 17.17. $C_7H_6O_4S$. Calculated %: C 45.15; H 3.24; S 17.22

Dimethyl 5-methyl-2,4-thiophene dicarboxylate (XII) was synthesized under conditions analogous to those for getting (IX), from 1.3 g of 5-methyl-2,4-thiophenedicarboxylic acid and 92 ml of an ether solution of diazomethane which contained about 2.24 g of diazomethane. We obtained 1.42 g (94.6%), m.p. 85-86° (from alcohol).

Found %: C 50.60, 50.66; H 4.91, 4.66; S 14.74, 14.81. $C_9H_{10}O_4S$. Calculated %: C 50.45; H 4.70. S 14.96.

SUMMARY

1. We have shown that 2,5-dimethylthiophene forms 3,4-diacetyl derivatives under conditions of the Friedel-Crafts reaction.

2. The yield of 2,5-dimethyl-3,4-diacetylthiophene can be increased by carrying out the acetylation without a solvent with an excess (2.5 moles) of aluminum chloride.

3. The structure of 2,5-dimethyl-3,4-diacetylthiophene was shown by its oxidation to 2,5-dimethyl-4-acetyl-3-thiophenecarboxylic acid, by decarboxylation of the latter into the known 2,5-dimethyl-3-acetothienone, and by oxidation of the diketone into the corresponding 3,4-dicarboxylic acid.

4. We have shown that 2-methyl- and 2-ethylthiophenes in the presence of excess acetyl chloride give the corresponding 3,5-diacetyl derivatives with yields on the order of 60%.

5. We have described a series of new mono- and difunctional derivatives of thiophene.

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THE CHEMISTRY OF SELENOPHENE

XXIX. 5-BROMO- AND 5-CHLOROSELENOPHENE-2-ALDEHYDE

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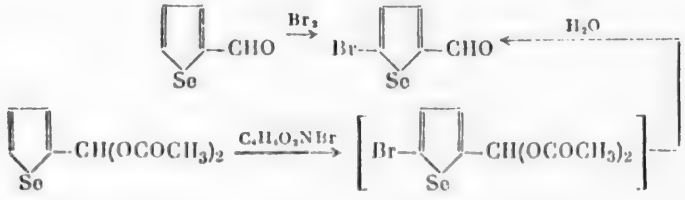
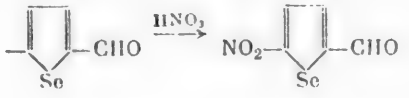
Continuing our study of the reactions of selenophene-2-aldehyde, we have investigated its relation to halogenating reagents and have obtained 5-halogenated selenophene-2-aldehydes.

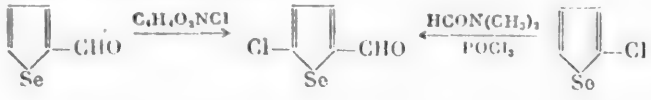
We obtained 5-bromoselenophene-2-aldehyde by bromination of selenophene-2-aldehyde with bromine, dioxane dibromide, and N-bromosuccinimide with yields of 23, 25, and 43% respectively. In recent work, Chierici and Pappalardo [1] described the synthesis of 5-bromoselenophene-2-aldehyde by formylation of 2-bromoselenophene with N-dimethylformamide which occurred only at the boiling temperature. This preparation of 5-bromoselenophene-2-aldehyde was identical with the preparation which we obtained by brominating selenophene-2-aldehyde diacetate with N-bromosuccinimide and later hydrolysis of the bromination product.



The ultraviolet absorption spectrum of the semicarbazones of 5-bromoselenophene-2-aldehyde (λ_{max} 324 mμ, lg ϵ_{max} 4.33) as given in Fig. 1 also agreed. The action of nitric acid on 5-bromoselenophene-2-aldehyde led to replacement of the bromine by the nitro group and the preparation of 5-nitroselenophene-2-aldehyde in a yield of 75%.



5-Chloroselenophene-2-aldehyde was obtained by chlorination of selenophene-2-aldehyde with N-chlorosuccinimide and by formylation of 2-chloroselenophene with dimethylformamide in the presence of phosphorus oxychloride with yields of 75% and 65% respectively.



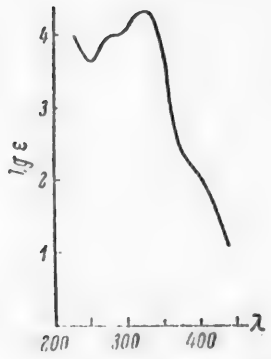


Fig. 1. Ultraviolet spectrum of 5-bromoselenophene-2-aldehyde semicarbazone (λ_{max} 324 mμ, lg ϵ_{max} 4.33).

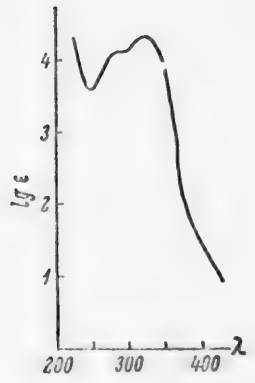
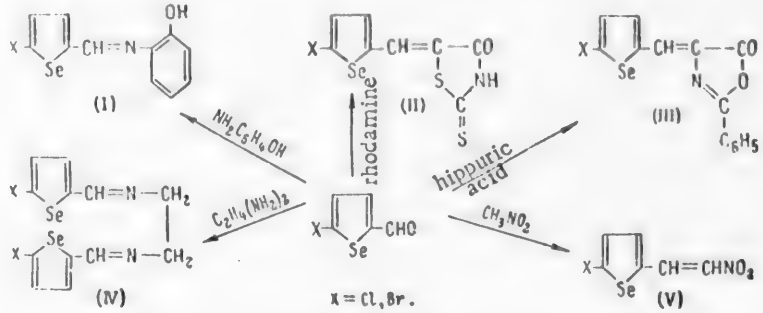


Fig. 2. Ultraviolet spectrum of 5-chloroselenophene-2-aldehyde semicarbazone (λ_{max} 321 mμ, lg ϵ_{max} 4.31).

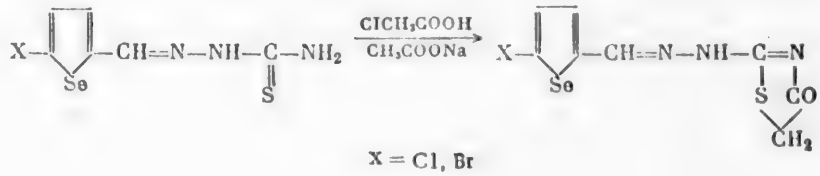
The curves of the ultraviolet absorption spectrum of the semicarbazone of both preparations of 5-chloroselenophene-2-aldehyde (λ_{max} 321 mμ, lg ϵ_{max} 4.31) as shown in Fig. 2 also agreed.

Thus, in chlorination or bromination of selenophene-2-aldehyde the halogen atom enters the 5 position of the selenophene ring.

The condensation of halogenated selenophenealdehydes with o-aminophenol, rhodanine, hippuric acid, ethylenediamine, and also nitromethane gave the corresponding N-(5-haloselenenal-2)-o-aminophenol (I), 5-(5'-haloselenenal-2')-4-thiazolidone-2-thione (II), 2-phenyl-5-(5'-haloselenenal-2')-4-oxazolone (III), N,N'-bis-(5-haloselenenal-2)-ethylenediamine (IV), and 5-halo-2-ω-nitrovinylselenophene (V).



The action of monochloroacetic acid on the thiosemicarbazone of 5-haloselenophene-2-aldehydes in the presence of sodium acetate led to preparation of hydrazothiazolinone-5-haloselenophene-2-aldehydes.



X = Cl, Br

EXPERIMENTAL

5-Bromoselenophene-2-aldehyde. a) To a boiling solution of 15 g of selenophene-2-aldehyde in 36 ml of dichloroethane (in the presence of traces of sulfur and hydroquinone) during 1.5 hours was added 17.3 g of

bromine in 45 ml of dichloroethane; the mixture was heated for one hour until evolution of hydrogen bromide stopped and then was steam distilled. The dichloroethane layer was separated and the water was extracted with ether. After distillation of the solvent from the solution dried over sodium sulfate the residue was distilled in a vacuum in a stream of nitrogen. We obtained 5 g (23%).

B.p. 112-113° (6 mm), nD^{20} 1.6719, d_4^{20} 2.1155.

b) To a solution of 11.9 g of selenophene-2-aldehyde in 25 ml of ether with stirring and cooling with water was added in portions 18.5 g of dioxane dibromide. Then the reaction mixture was washed with water, with soda, again with water and the ether solution was dried with sodium sulfate. After the ether had been distilled off, the residue was distilled in a vacuum in a stream of nitrogen. We obtained 4.5 g (25%).

B.p. 114-115° (7 mm), nD^{20} 1.6712, d_4^{20} 2.1159.

c) To a boiling solution of 32 g of selenophene-2-aldehyde in 100 ml of dry chloroform with energetic stirring was added 40 g of N-bromosuccinimide, heating was continued for one hour, and the product was steam distilled. After treatment of the distillate as described in (a) we obtained 20.5 g (43%).

B.p. 124-125° (12 mm), nD^{20} 1.6728, d_4^{20} 2.1168, MR_D 42.16. $C_5H_3BrOSe_{F2}$. Calculated 40.57; EM_D 1.59.

Found %: C 24.74, 24.66; H 2.28, 2.18. $C_6H_6ON_3BrSe$. Calculated %: C 24.41; H 2.03.

Literature data [1]: b.p. 110° (15 mm).

Semicarbazone, m.p. 200-201° (with decomposition, from 50% alcohol); glittering light-yellow platelike crystals.

Found %: C 25.12, 25.35; H 1.45, 1.43; Se 33.21, 33.28. C_5H_3OBrSe. Calculated %: C 25.23; H 1.28; Se 33.59.

Oxime: m.p. 132-133° (with decomposition, from 30% alcohol) silky, needle-like crystals.

Found %: C 24.13, 23.99; H 1.82, 1.91. $C_5H_4ONBrSe$. Calculated %: C 23.17; H 1.58.

2,4-Dinitrophenylhydrazone, m.p. 247-248° (from a mixture of alcohol and ethyl acetate, 1 : 2), bright-red crystals.

Found %: C 31.37, 31.47; H 1.93, 1.89. $C_{11}H_7O_4N_4BrSe$. Calculated %: C 31.60; H 1.69.

Thiosemicarbazone, m.p. 175-176° (from 50% alcohol), yellow crystals.

Found %: C 23.39, 23.28; H 2.03, 1.84. $C_6H_6N_3BrSSe$. Calculated %: C 23.17; H 1.94.

Selenophene-2-aldehyde diacetate. A mixture of 10 g of selenophene-2-aldehyde, 6.5 g of acetic anhydride and 0.3 g of anhydrous zinc chloride remained at 20° for 24 hours; the precipitate was washed with water and with soda. We obtained 15.3 g (95%); m.p. 58-59° (from alcohol), white hexagonal crystals.

Found %: C 41.29, 41.49; H 3.74, 3.68; Se 30.00, 29.91. $C_9H_{10}O_4Se$. Calculated %: C 41.39; H 3.86; Se 30.24.

Bromination of selenophene-2-aldehyde diacetate. To a boiling solution of 7.5 g of selenophene-2-aldehyde diacetate in 20 ml of dry chloroform with stirring was added 5.3 g of N-bromosuccinimide, the mixture was heated for one hour and steam distilled. After treatment of the distillate as described in (a) we obtained 4.5 g (63%) of 5-bromoselenophene-2-aldehyde.

B.p. 114-115° (7 mm), nD^{20} 1.6719, d_4^{20} 2.1157.

5-Nitroselenophene-2-aldehyde. A mixture of 2.4 g of 5-bromoselenophene-2-aldehyde and 7 ml of nitric acid (d 1.2) was heated to the beginning of the exothermal reaction; after the violent reaction, the mixture was heated for two hours until vapors of bromine disappeared, and was diluted threefold with water. The precipitate was filtered and washed. We obtained 1.4 g (70%); m.p. 88° (from ligroin), light-yellow needles. A sample mixed with commercial 5-nitroselenophene-2-aldehyde [2] gave no melting point depression. According to the literature [2], m.p. 89°.

2-Chloroselenophene. To 30 g of selenophene was added over ten minutes 32.4 g of sulfuryl chloride, the mixture was boiled one hour and steam distilled. The distillate was extracted with ether; the extract was dried with sodium sulfate. The ether was distilled off, and the residue was fractionated. We obtained 16.5 g (60%).

B.p. 152-153° (740 mm); nD^{20} 1.5939, d_4^{20} 1.7560, MR_D 32.1. $C_4H_3ClSe_{F2}$. Calculated 33.0.

Found %: C 29.14, 29.09; H 1.90, 1.92; Se 47.42, 47.30. C_4H_3ClSe. Calculated %: C 29.03; H 1.83; Se 47.71.

Literature data [3]: B.p. 42° (14.5 mm), nD^{20} 1.5940, d_4^{20} 1.6621.

5-Chloroselenophene-2-aldehyde. a) To a boiling solution of 5 g of selenophene-2-aldehyde in 20 ml of dry chloroform was added 5 g of N-chlorosuccinimide; it was heated for 30 minutes, cooled, the succinimide was filtered off and washed with chloroform. After distillation of the solvent the residue was distilled in a vacuum. We obtained 4.5 g (75%).

B.p. 93° (5 mm), nD^{20} 1.6419, d_4^{20} 1.7840, MR_D 38.80. $C_5H_3OClSe_{F2}$. Calculated 37.67; EM_D 1.13.

Found %: C 31.23, 31.25; H 1.47, 1.67; Se 40.42, 40.53. C_5H_3OClSe. Calculated %: 31.03; H 1.52; Se 40.80.

b) To a mixture of 32.3 g of 2-chloroselenophene and 20 g of dimethylformamide with stirring and cooling by ice water was added over 1.5 hours 43 g of phosphorus oxychloride; it was stirred at 65° for one hour, cooled, poured onto ice (500 g) and 375 g of sodium acetate was added; it was heated to complete solution and extracted with ether. The extract was dried over sodium sulfate, the ether was distilled off, and the residue distilled in a vacuum. We obtained 25 g (65%).

B.p. 97.5° (8 mm), nD^{20} 1.6419, d_4^{20} 1.7842.

Semicarbazone; m.p. 196-197° (from 80% alcohol), light-yellow, glittering plates.

Found %: C 29.10, 29.15; H 2.60, 2.71. $C_6H_6ON_3ClSe$. Calculated %: C 28.75; H 2.41.

Oxime; m.p. 114-115° (from 60% alcohol).

Found %: C 29.10, 29.27; H 1.99, 2.00. $C_5H_4ONClSe$. Calculated %: C 28.79; H 1.94.

Thiosemicarbazone; m.p. 170° (from 50% alcohol), light-yellow crystals.

Found %: C 27.22, 27.15; H 2.37, 2.45. $C_6H_6N_3ClSSe$. Calculated %: C 27.02; H 2.27.

5-Bromo-2-ω-nitrovinylselenophene. To a solution of 3.75 g of 5-bromoselenophene-2-aldehyde and 1.22 g of nitromethane in 10 ml of methyl alcohol with cooling (by snow and salt) and energetic stirring we added dropwise a solution of 0.6 g of sodium hydroxide in 4 ml of water; stirring was continued for 30 minutes more, 20 ml of water was added, it was well cooled and 6 ml of 10% hydrochloric acid was added dropwise, it was cooled to -5° (not above 0°). The precipitate was separated and washed with ice water. We obtained 2 g (46%); m.p. 111-112° (from 75% alcohol), glittering yellow needles.

Found %: C 25.17, 25.27; H 1.59, 1.75; Se 27.88, 27.76. $C_6H_4O_2NBrSe$. Calculated %: C 25.64; H 1.44; Se 28.10.

5-Chloro-2-ω-nitrovinylselenophene. From 1.93 g of 5-chloroselenophene-2-aldehyde and 1.22 g of nitromethane we obtained as described above 1.5 g (66%); m.p. 106-107° (from 75% alcohol), yellow crystals.

Found %: C 30.28, 30.17; H 1.81, 1.94; Se 33.02, 32.90. $C_6H_4O_2NClSe$. Calculated %: C 30.46; H 1.70; Se 33.36.

N-(5-Bromoselenenal-2)-o-aminophenol. A solution of 2.38 g of 5-bromoselenophene-2-aldehyde and 1.18 g of o-aminophenol in 20 ml of methyl alcohol was heated for two hours on a water-bath. After distillation of part of the alcohol, a precipitate came down; we obtained 3.2 g (93%); m.p. 65-66° (from 50% alcohol), yellow crystals.

Found %: C 39.90, 39.82; H 2.23, 2.17; Se 23.66, 23.54. $C_{11}H_8ONBrSe$. Calculated %: C 40.14; H 2.45; Se 23.99.

N-(5-Chloroselenenal-2)-o-aminophenol. From 1.93 g of 5-chloroselenophene-2-aldehyde and 1.18 g of o-aminophenol we obtained 2.3 g (81%); m.p. 58-59° (from 70% alcohol); light-yellow crystals.

Found %: C 46.28, 46.17; H 2.57, 2.65; Se 27.38, 27.43. $C_{11}H_8ONClSe$. Calculated %: C 46.42; H 2.83; Se 27.74.

N,N'-Bis(5-bromoselenenal-2)-ethylenediamine. To 2.38 g of 5-bromoselenophene-2-aldehyde was added 3.4 ml of 20% aqueous solution of ethylenediamine, 10 ml of alcohol, and the mixture was heated for three hours on a water bath. We obtained 1.2 g (48%); m.p. 121-122° (from 50% alcohol).

Found %: C 28.79, 29.21; H 2.10, 1.88; Se 31.25, 31.33. $C_{12}H_{10}N_2Br_2Se_2$. Calculated %: C 28.82; H 2.02; S 31.58.

N,N'-Bis(5-chloroselenenal-2)-ethylenediamine. Form 1.93 g of 5-chloroselenophene-2-aldehyde and 3.4 ml of 20% aqueous solution of ethylenediamine we obtained 1.4 g (68%); m.p. 105-106° (from 50% alcohol).

Found %: C 34.84, 34.79; H 2.57, 2.70; Se 38.09, 38.20. $C_{12}H_{10}N_2Cl_2Se_2$. Calculated %: C 35.05; H 2.45; Se 38.41.

2-Phenyl-5-(5'-bromoselenenal-2')-4-oxazolone. A mixture of 0.8 g of 5-bromoselenophene-2-aldehyde, 0.6 g of hippuric acid, 0.3 g of anhydrous sodium acetate, and 3.3 g of acetic anhydride was heated on a water bath for one hour. We obtained 1.1 g (87%); m.p. 182-183° (from benzene), yellow needles.

Found %: C 44.24, 44.01; H 2.68, 2.50; Se 20.43, 20.31. $C_{14}H_8O_2NBrSe$. Calculated %: C 44.12; H 2.38; Se 20.71.

2-Phenyl-5-(5'-chloroselenenal-2')-4-oxazolone. From 1.93 g of 5-chloroselenophene-2-aldehyde, 1.78 g of hippuric acid, 0.8 g of anhydrous sodium acetate, and 10 g of acetic anhydride we obtained 3.27 g (97%); m.p. 173-174° (from benzene), yellow needles.

Found %: C 50.34, 50.41; H 2.50, 2.65; Se 23.01, 23.12. $C_{14}H_8O_2NClSe$. Calculated %: C 49.99; H 2.33; Se 23.45.

5-(5'-Bromoselenenal-2')-4-thiazolidone-2-thione. To a slightly heated solution of 2.38 g of 5-bromoselenophene-2-aldehyde and 1.3 g of rhodanine in 8.8 ml of glacial acetic acid was added 1.85 g of anhydrous sodium acetate; the mixture was heated 0.5 hour and 50 ml of water was added. The precipitate was washed with water, alcohol, and ether. We obtained 1.5 g (43%) of glittering light-brown crystals which decomposed without melting.

Found %: C 27.69, 27.75; H 1.38, 1.40; Se 22.01, 21.92. $C_8H_4ONBrS_2Se$. Calculated %: C 27.50; H 1.15; Se 22.36.

5-(5'-Chloroselenenal-2')-4-thiazolidone-2-thione. From 1.93 g of 5-chloroselenophene-2-aldehyde, 1.3 g of rhodanine in 8.8 ml of glacial acetic acid, and 1.85 g of anhydrous sodium acetate we obtained 1.4 g (45%); m.p. 243° (decomposition), glittering light-brown crystals.

Found %: C 31.16, 31.06; H 1.39, 1.38; Se 25.17, 25.22. $C_7H_4ONClS_2Se$. Calculated %: C 31.12; H 1.31; Se 25.54.

Hydrazothiazolinone-5-bromoselenophene-2-aldehyde. To 1.51 g of the thiosemicarbazone of 5-bromoselenophene-2-aldehyde in 20 ml of alcohol was added 1 g of chloroacetic acid and the mixture was heated for one hour. The precipitate was washed with hot water and alcohol. We obtained 1.4 g (80%); m.p. 243° (decomposition).

Found %: C 27.08, 27.15; H 1.63, 1.84; Se 22.04, 22.19. $C_8H_5ON_3BrSSe$. Calculated %: C 27.36; H 1.72; Se 22.49.

Hydrazothiazolinone-5-chloroselenophene-2-aldehyde. From 1.33 g of the thiosemicarbazone of 5-chloroselenophene-2-aldehyde, 1 g of anhydrous sodium acetate, and 1 g of chloroacetic acid we obtained 1.4 g (91%); m.p. 241° (decomposition).

Found %: C 30.68, 30.90; H 2.11, 2.03; Se 25.46, 25.38. $C_8H_6ON_3ClSSe$. Calculated %: H 1.97; Se 25.75.

SUMMARY

1. By bromination of selenophene-2-aldehyde with bromine, dioxane dibromide, and N-bromosuccinimide, as well as by bromination of selenophene-2-aldehyde diacetate with N-bromosuccinimide we obtained 5-bromoselenophene-2-aldehyde.

2. Chlorination of selenophene-2-aldehyde with N-chlorosuccinimide and formylation of 2-chloroselenophene with dimethylformamide give 5-chloroselenophene-2-aldehyde.

3. 5-Bromo- and 5-chloroselenophene-2-aldehydes react easily with nitromethane, hippuric acid, o-aminophenol, ethylenediamine, and rhodanine, to form the corresponding selenenal derivatives: condensation of the thiosemicarbazone of 5-haloselenophene-2-aldehydes with chloroacetic acid also gives the corresponding selenenal derivatives.

4. When nitric acid acts on 5-bromoselenophene-2-aldehyde the nitro group replaces the bromine to give 5-nitroselenophene-2-aldehyde.

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THE CHEMISTRY OF SELENOPHENE

XXX. CHOROMETHYLATION OF KETONES OF THE SELENOPHENE SERIES

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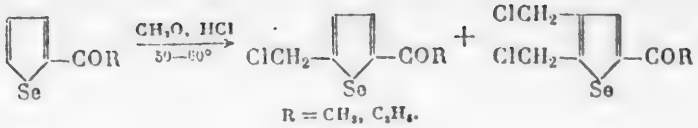
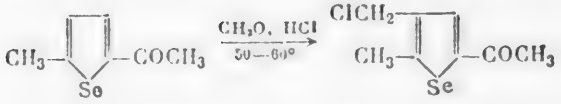
The reaction of chloromethylation of ketones of the aromatic and heterocyclic series has been little studied. In 1920 Stephen [1] carried out the chloromethylation of anthraquinone by chloromethyl esters in the presence of zinc chloride but did not obtain positive results. Later attempts at chloromethylation of acetophenone [2] and benzophenone [3] were also without result. Fuson and Keever [3] using paraform and concentrated hydrochloric acid succeeded in carrying out the chloromethylation of some aromatic ketones which had two or more alkyl groups in the benzene ring. They showed that in these ketones the chloromethyl group replaced hydrogen in the aromatic ring and not on the α-carbon atom of the acyl group. In 1956 the chloromethylation of 2-hydroxy- and 2-methoxypropiophenone was carried out [4] and along with the monochloromethyl derivative were obtained dichloromethyl derivatives; in these cases the chloromethyl groups also replaced hydrogen of the benzene ring. According to the results of Hartough [5] in the chloromethylation of 2-acetothiophene by formalin and concentrated hydrochloric acid, β-chloropropiothiophene and α-chloromethyl-β-chloropropiothiophene are obtained.

In the present work, a continuation of the study of reactions of ketones of the selenophene series, we have carried out chloromethylation of 2-aceto-, 2-propio-, and 2-methyl-5-acetoselenophene. By changing the reaction conditions we have succeeded in finding ones in which the yield of chloromethyl derivatives reaches 74-80% based on the ketone used. For this purpose we must have a threefold excess of 34% formalin and concentrated hydrochloric acid, a rapid stream of hydrogen chloride and a temperature of 50-60° while continuing the reaction 5-5.5 hours in dichloroethane as the solvent. When formalin is replaced by paraform the yield of chloromethyl derivative of 2-acetoselenophene is 70%. Monochloromethyl derivatives of 2-aceto- and 2-propioselenophene as a rule are obtained with small admixtures of dichloromethyl derivatives which can be separated by distillation. Decreasing the amount of dichloroethane to a minimum causes a sharp change in the ratio of substances formed in the direction of an increase in the dichloromethyl derivatives: in this case, with chloromethylation of 2-acetoselenophenone we obtained 41% of the monochloromethyl derivative instead of 74%, and 16% of the dichloromethyl derivative instead of a trace; in the analogous chloromethylation of 2-propioselenophene we obtained 36% of the monochloromethyl derivative instead of 80%, and 24% of the dichloromethyl derivative instead of a trace.

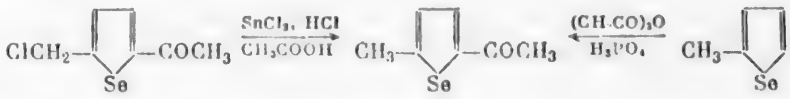
We can expect that by analogy with the behavior of 2-acetothiophene in this reaction the products of monochloromethylation of 2-aceto- and 2-propioselenophene will have the structure of β-chloropropioselenophene and the corresponding β-chloro-α-chloromethylpropioselenophene. In this case their reaction with dimethylamine should give aminoketones identical with those which two of us obtained previously [6] in the Mannich reaction in aminomethylation of 2-aceto- and 2-propioselenophenes. However, a mixed sample of the hydrochlorides of the two aminoketones obtained in this way from 2-acetoselenophene showed a depression of 40°; for the hydrochlorides of the two aminoketones from 2-propioselenophene the depression was 25°. Hence, chloromethylation of ketones of the selenophene series occurs in the selenophene ring and not on the α-hydrogen atom of the acyl group.



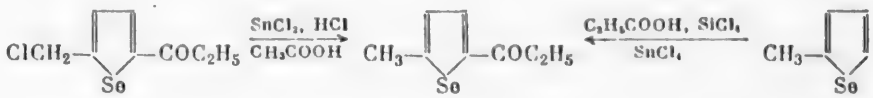
R = CH_3, C_2H_5.



As evidence of the structure of the 2-chloromethyl-5-acetoselenophene obtained in this way we have the reduction of it by tin chloride to 2-methyl-5-acetoselenophene, identical with that obtained by acetylation of 2-methylselenophene.

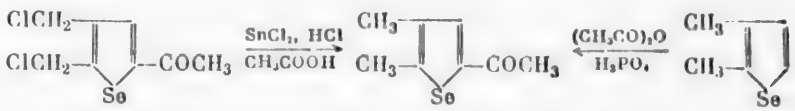


In the same way we have shown the structure of 2-chloromethyl-5-propioselenophene. By reduction of this ketone with tin chloride we have obtained 2-methyl-5-propioselenophene, identical with the 2-methyl-5-propioselenophene obtained by acylation of 2-methylselenophene.

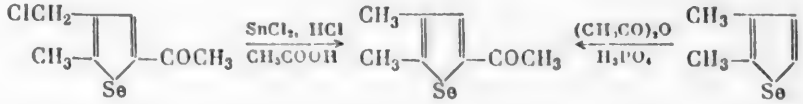


As to the structure of the dichloromethyl derivatives of 2-acetoselenophene, we can expect that the second chloromethyl group will enter the ortho position with respect to the first and the meta position with respect to the acyl group, that is, the dichloromethyl derivative should have the structure of 2,3-di(chloromethyl)-5-acetoselenophene.

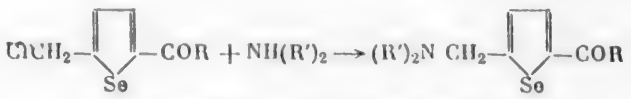
By reduction of 2,3-di(chloromethyl)-5-acetoselenophene with tin chloride we get 2,3-dimethyl-5-acetoselenophene which is identical with the 2,3-dimethyl-5-acetoselenophene obtained by direct synthesis.



In an analogous way from 2-methyl-5-acetoselenophene by the chloromethylation reaction we can form 2-methyl-3-chloromethyl-5-acetoselenophene. Actually, in the reduction of the latter we obtain 2,3-dimethyl-5-acetoselenophene which is identical with the 2,3-dimethyl-5-acetoselenophene obtained by direct synthesis.



2-Chloromethyl-5-acetoselenophene and 2-chloromethyl-5-propioselenophene react easily with dimethyl- and diethylamines with formation of the corresponding tertiary amines.



R = CH_3, C_2H_5; R′ = CH_3, C_2H_5.

EXPERIMENTAL

Chloromethylation of ketones of the selenophene series was carried out in a four-neck flask with a stirrer, gas inlet tube, reflux condenser, and thermometer. Into the mixture of ketone, 34% formalin, concentrated hydrochloric acid, and dichloroethane was passed a rapid stream of hydrogen chloride for 5-5.5 hours at 50-60°; the mixture quickly darkened and became red brown. When the mixture had cooled, air was passed through it for 15-20 minutes and it was poured into cold water. An oily layer separated, the water layer was repeatedly extracted with dichloroethane, the extracts and the oily layer were combined, washed with 2 N sodium hydroxide to a weakly alkaline reaction of the wash water, which was twice extracted with dichloroethane. The dichloroethane solution was dried over potash, the solvent was distilled off, and the substance was distilled in a vacuum.

2-Chloromethyl-5-acetoselenophene. Eight g of 2-acetoselenophene, 11 ml of 34% formalin, 11 ml of concentrated hydrochloric acid, 50 ml of dichloroethane, a stream of hydrogen chloride. We recovered 1.8 g of unchanged ketone. We obtained 5.9 g (74% based on ketone used).

B.p. 144.5-145.5 (8 mm), nD^{20} 1.6118, d_4^{20} 1.5982, MR_D 48.19. $C_7H_7OClSe_{F2}$. Calculated 46.87.

Found %: C 37.94, 37.76; H 3.20, 3.32; Se 35.96, 35.81. C_7H_7OClSe. Calculated %: C 37.94; H 3.18; Se 35.64.

2,3-Di(chloromethyl)-5-acetoselenophene. Eight g of 2-acetoselenophene, 11 ml of 34% formalin, 11 ml of concentrated hydrochloric acid, 10 ml of dichloroethane, a stream of hydrogen chloride. We obtained 4.2 g (41%) of 2-chloromethyl-5-acetoselenophene with b.p. 143-145° (8 mm) and 2.4 g (16%) of 2,3-di(chloromethyl)-5-acetoselenophene with m.p. 70-71° (from 50% alcohol).

Found %: C 35.74, 35.66; H 2.93, 2.90; Se 29.48, 29.36. $C_8H_8OCl_2Se$. Calculated %: C 35.58; H 2.98; Se 29.22.

2-Chloromethyl-5-propioselenophene. Fifteen g of 2-propioselenophene, 28 ml of 34% formalin, 21 ml of concentrated hydrochloric acid, 50 ml of dichloroethane, a stream of hydrogen chloride. We recovered 4.9 g of unchanged ketone. We obtained 9 g (80%, based on ketone used).

B.p. 148.5-149.5° (8 mm), nD^{20} 1.5969, d_4^{20} 1.5212, MR_D 52.74. $C_8H_9OClSe_{F2}$. Calculated 51.49.

Found %: C 41.35, 41.16; H 3.72, 3.84; Se 33.45, 33.71. C_8H_9OClSe. Calculated %: C 40.81; H 3.85; Se 33.53.

2,3-Di(chloromethyl)-5-propioselenophene. Ten g of 2-propioselenophene, 25 ml of 34% formalin, 14 ml of concentrated hydrochloric acid, 5 ml of dichloroethane, a stream of hydrogen chloride. We obtained 4.5 g (36%) of 2-chloromethyl-5-propioselenophene with b.p. 148-150° (8 mm) and 3.65 g (24%) of 2,3-di(chloromethyl)-5-propioselenophene with m.p. 79-80° (from 50% alcohol).

Found %: C 38.50, 38.71; H 3.67, 3.86; Se 27.47, 27.59. $C_9H_{10}OCl_2Se$. Calculated %: C 38.05; H 3.55; Se 27.81.

2-Methyl-3-chloromethyl-5-acetoselenophene. A mixture of 8.6 g of 2-methyl-5-acetoselenophene, 11 ml of 34% formalin, 11 ml of concentrated hydrochloric acid, 50 ml of dichloroethane, a stream of hydrogen chloride. We obtained 8.7 g (80%).

B.p. 182-183° (19 mm), m.p. 69-70°.

Found %: C 40.65, 40.70; H 3.98, 3.80; Se 33.31, 33.26. C_8H_9OClSe. Calculated %: C 40.81; H 3.85; Se 33.53.

2-Diethylaminomethyl-5-acetoselenophene. In a three-neck flask with a stirrer and reflux condenser we placed 6 g of 2-chloromethyl-5-acetoselenophene, 6.75 g of diethylamine, and 2.7 g of powdered potash. After the exothermal reaction had ended, the mixture was heated for three hours on the water bath, cooled, poured into water, and repeatedly extracted with benzene. The extract was dried with potash and unchanged diethylamine and benzene were distilled off and the residue was distilled in a vacuum. We obtained 6.15 g (88%).

B.p. 153-153.5° (8 mm), nD^{20} 1.5544, d_4^{20} 1.2582, MR_D 65.82. $C_{11}H_{17}ONSe_{F2}$. Calculated 64.42.

Found %: C 51.08, 50.95; H 6.56, 6.88; Se 30.41, 30.26. $C_{11}H_{17}ONSe$. Calculated %: C 51.17; H 6.64; Se 30.59.

Picrate; m.p. 97-98° (from 50% alcohol).

Found %: C 41.94, 41.74; H 4.23, 4.05; Se 16.33, 16.53. $C_{17}H_{20}O_8N_4Se$. Calculated %: C 41.90; H 4.14; Se. 16.20.

Hydrochloride; m.p. 163-164° (after reprecipitation by absolute ether from anhydrous alcohol).

Found %: C 44.55, 44.57; H 6.08, 6.01; Se 26.97, 27.12. $C_{11}H_{18}ONClSe$. Calculated %: C 44.83; H 6.16; Se 26.80.

2-Diethylaminomethyl-5-propioselenophene. From 6.2 g of 2-chloromethyl-5-propioselenophene, 4.7 g of diethylamine, and 1.9 g of potash we obtained as described above 5.5 g (70%).

B.p. 156-157° (8 mm), nD^{20} 1.5480, d_4^{20} 1.2282, MR_D 70.41. $C_{12}H_{19}ONSe_{F2}$. Calculated 69.04.

Found %: C 52.67, 52.49; H 6.71, 6.04; Se 28.64, 28.81. $C_{12}H_{19}ONSe$. Calculated %: C 52.94; H 7.03; Se 29.00.

Picrate; m.p. 127-128° (from 50% alcohol).

Found %: C 43.23, 43.30; H 4.20, 4.33; Se 15.78, 15.54. $C_{18}H_{22}O_8N_4Se$. Calculated %: C 43.10; H 4.42; Se 15.75.

Hydrochloride; m.p. 150.5-151.5° (after reprecipitation by anhydrous alcohol from absolute ether).

Found %: C 46.59, 46.65; H 6.41, 6.29; Se 25.80, 25.61. $C_{12}H_{20}ONClSe$. Calculated %: C 46.68; H 6.53; Se 25.58.

2-Dimethylamino-5-acetoselenophene. Into a mixture of 6 g of 2-chloromethyl-5-acetoselenophene, 7.4 g of powdered potash, 15 ml of dichloroethane, heated for three hours on a water bath at 50-70° we passed dimethylamine. After cooling, the mixture was poured into water and repeatedly extracted with dichloroethane. The extract was dried with potash, the solvent was distilled off, and the residue was distilled in a vacuum. We obtained 4.8 g (78%).

B.p. 137-137.5° (8 mm), nD^{20} 1.5683, d_4^{20} 1.3322, MR_D 56.56. $C_9H_{13}ONSe_{F2}$. Calculated 55.18.

Found %: C 46.95, 46.99; H 5.91, 5.91; Se 34.51, 34.40. $C_9H_{13}ONSe$. Calculated %: C 46.96; H 5.69; Se 34.32.

Picrate; m.p. 129-130° (from 50% alcohol).

Found %: C 39.17, 39.17; H 3.71, 3.75; Se 17.42, 17.00. $C_{15}H_{16}O_8N_4Se$. Calculated %: C 39.22; H 3.51; Se 17.19.

Hydrochloride; m.p. 159.5-160.5° (after reprecipitation by absolute ether from anhydrous alcohol).

Found %: C 40.20, 40.33; H 5.14, 5.21; Se 29.44, 29.72. $C_9H_{14}ONClSe$. Calculated %: C 40.54; H 5.29; Se 29.68.

2-Dimethylamino-5-propioselenophene. As described above, from 6 g of 2-chloromethyl-5-propioselenophene, 7.3 g of potash in 15 ml of dichloroethane, with passing of dimethylamine for 2.5 hours, we obtained 5 g (80%).

B.p. 153-154° (10 mm), nD^{20} 1.5569, d_4^{20} 1.2872, MR_D 61.08. $C_{10}H_{15}ONSe_{F2}$. Calculated 59.80.

Found %: C 49.38, 49.50; H 6.15, 6.26; Se 32.01, 32.20. $C_{10}H_{15}ONSe$. Calculated %: C 49.19; H 6.19; Se 32.34.

Picrate; m.p. 97-98° (from 50% alcohol).

Found %: C 40.44, 40.52; H 3.52, 3.70; Se 16.54, 16.40. $C_{16}H_{18}O_8N_2Se$. Calculated %: C 40.61; H 3.83; Se 16.69.

Hydrochloride; m.p. 168-168.5° (after reprecipitation by absolute ether from anhydrous alcohol).

Found %: C 42.64, 42.54; H 5.41, 5.72; Se 28.43, 28.51. $C_{10}H_{16}ONClSe$. Calculated %: C 42.78; H 5.74; Se 28.19.

2-Methyl-5-acetoselenophene. In a mixture of 27 g of tin chloride and 54 ml of acetic acid was passed hydrogen chloride to full solution (20-30 minutes); the solution was filtered and 6 g of 2-chloromethyl-5-acetoselenophene was added dropwise; the mixture stood for 48 hours and was poured into 150 ml of water and extracted with ether. The ether extract was washed with 40% sodium hydroxide and dried with calcium chloride. By distillation we obtained 0.5 g (10%); b.p. 114-116° (12 mm).

Semicarbazone: m.p. 218-219° (from 50% alcohol).

A sample mixed with a commercial semicarbazone of 2-methyl-5-acetoselenophene obtained by acetylation of 2-methylselenophene showed no depression of the melting point. The literature [7] gives m.p. 219-220°.

2-Methyl-5-propioselenophene. a) By the method of [8] from 6 g of 2-methylselenophene, 6.13 g of propionic acid, and 47 g of silicon tetrachloride in the presence of 5.4 g of anhydrous tin chloride in 50 ml of anhydrous benzene we obtained 2.8 g (33%); b.p. 119-121° (12 mm), m.p. 33-33.5° (from 50% alcohol).

b) From 8 g of 2-chloromethyl-5-propioselenophene and 34 g of tin chloride in 70 ml of acetic acid we obtained as described above 1.7 g (25%); m.p. 33-34° (from 50% alcohol).

A sample mixed with commercial 2-methyl-5-propioselenophene gave no depression of the melting point.

Found %: C 48.29, 48.06; H 4.89, 4.77; Se 38.97, 39.13. $C_8H_{10}OSe$. Calculated %: C 47.78; H 5.01; Se 39.26.

Semicarbazone: m.p. 200-201.5° (from 50% alcohol).

Found %: C 42.44, 42.20; H 5.00, 4.98; Se 30.42, 30.28. $C_9H_{13}ON_3Se$. Calculated %: C 41.87; H 5.07; Se 30.59.

2,4-Dinitrophenylhydrazone: m.p. 227-227.5° (from a mixture of alcohol and ethyl acetate).

Found %: C 43.74, 43.74; H 3.74, 3.57; Se 21.02, 20.91. $C_{14}H_{14}O_4N_4Se$. Calculated %: C 44.10; H 3.70; Se 20.66.

2,3-Dimethyl-5-acetoselenophene. a) By acetylation of 9.5 g of 2,3-dimethylselenophene with 3.4 g of acetic anhydride and a mixture of 0.7 g of 85% phosphoric acid and 3.4 g of acetic anhydride by the method of [7] we obtained 7.6 g (63%).

Found %: C 47.96, 48.03; H 5.23, 5.34; Se 39.38, 39.45. $C_8H_{10}OSe$. Calculated %: C 47.78; H 5.01; Se 39.26.

B.p. 133-134° (15 mm), nD^{20} 1.5865, d_4^{20} 1.4042, MR_D 48.09. $C_8H_{10}OSeF_2$. Calculated 46.63.

2,4-Dinitrophenylhydrazone: m.p. 261-262° (from a mixture of alcohol and amyl acetate).

Found %: C 43.84, 43.61; H 3.93, 3.96; Se 20.58, 20.64. $C_{14}H_{14}O_4N_4Se$. Calculated %: C 44.10; H 3.70; Se 20.66.

b) From 4 g of 2,3-di(chloromethyl)-5-acetoselenophene and 30 g of tin chloride in 60 ml of acetic acid as described above we obtained 0.4 g (13%); b.p. 130-132° (13 mm).

2,4-Dinitrophenylhydrazone: m.p. 261-262° (from a mixture of alcohol and amyl acetate). A sample mixed with commercial 2,4-dinitrophenylhydrazone of 2,3-dimethyl-5-acetoselenophene showed no depression of the melting point.

c) From 7 g of 2-methyl-3-chloromethyl-5-acetoselenophene and 29 g of tin chloride in 60 ml of acetic acid, as described above, we obtained 1.5 g (25%); b.p. 148-150° (22 mm).

2,4-Dinitrophenylhydrazone: m.p. 261-262° (from a mixture of alcohol and amyl acetate). A sample mixed with commercial 2,4-dinitrophenylhydrazone of 2,3-dimethyl-5-acetoselenophene gave no depression of the melting point.

SUMMARY

1. In chloromethylation of 2-acylselenophenes the chloromethyl group replaces a hydrogen of the selenophene ring; depending on the reaction conditions one chloromethyl group enters the ring in the unsubstituted 5-

position, and if this is occupied, then in the unsubstituted 4-position, or two chloromethyl groups enter in unsubstituted 4 and 5 positions. Thus we have obtained 2-chloromethyl-5-acetoselenophene, 2,3-di(chloromethyl)-5-acetoselenophene, 2-chloromethyl-5-propioselenophene, 2,3-di(chloromethyl)-5-propioselenophene, and 2-methyl-3-chloromethyl-5-acetoselenophene.

2. The reaction of 2-chloromethyl-5-acetoselenophene and 2-chloromethyl-5-propioselenophene with dimethyl- and diethylamine leads to the corresponding tertiary amine, the 2-dialkylaminomethyl-5-acetoselenophene.

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THE ABSORPTION SPECTRA OF DISUBSTITUTED BENZENES WITH FUNCTIONAL GROUPS OF SIMILAR DIRECTING POWER

III. NITROBENZOIC ACIDS AND ETHYL NITROBENZOATES

A. E. Lutskii and V. T. Alekseeva

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The absorption curves for disubstituted benzenes with the composition AC_6H_4A or DC_6H_4D (where A is an electron acceptor, and D an electron donor) actually differ from those of disubstituted compounds AC_6H_4D by the absence in the first of a band due to transfer of an excited charge with participation in this transfer of π - and p-electrons of both functional groups and the comparatively small dependence of the curves on the relative position of the substituents [1]. For a further test of this fact we measured the position in the middle ultraviolet of o-, m, and p-nitrobenzoic acids and their ethyl esters in hexane (for the latter), benzene, dioxane, diethyl ether, n-butanol, 98% sulfuric acid, diluted 9.8% sulfuric acid, and nitrobenzoic acid in 2 N alkali (NaOH). The absorption curves in some of the solvents studied are given in Figs. 1-6, the rest in another place [2]; the values for the wavelength (λ) and extinction (ϵ) of shoulders and maxima of the curves in all the solvents are given in Table 1. These values as a rule agree well with the existing data for band B (or shoulders) from other authors [3-5].

The absorption curves of these compounds in nonpolar solvents (hexane and dioxane) consist of long wave, low intensity shoulders between 310-354 mμ ($\lg \epsilon$ 2.00-2.50) and intense bands (sometimes appearing only as shoulders) as a rule in the region of 250-255 mμ ($\lg \epsilon$ 3.9-4.6). They almost agree in their positions with those in unsubstituted nitrobenzene whose curve in hexane (heptane) also consists of shoulders at about 330 mμ ($\lg \epsilon$ 2.1) and bands with maxima at 251 mμ ($\lg \epsilon$ 4.0) [1, 6, 7]. In the esters in hexane there also appear on the absorption curves the bands of nitrobenzene in this solvent at 280 mμ and $\lg \epsilon$ 3.0. Evidently in nitrobenzoic acids and their esters the absorption curves are analogous to that of nitrobenzene [8], that is, absorption in them is determined chiefly by the same electron transfers as in the latter, and the shoulders are connected with $p \rightarrow \pi^*$ (or $\pi \rightarrow \pi^*$) transfers localized in the nitro group, while the bands are caused not by transfers $A_{1g} \rightarrow B_{2n}$ in the ring [3, 5], but by transfers of the charge from the ring to the nitro group [1, 9, 10]. Evidence for this comes from the similar character of the change in absorption curves of these compounds in nitrobenzene with change in the medium. Thus, in the presence of alkali there occurs in nitrobenzoic acid not a shift to the short wave as is found for bands connected with transfers characteristic of participation in them of electrons of the carboxyl group [3, 11], but a shift toward the long waves, and the bands have maxima (λ 270-273 mμ, $\lg \epsilon$ 3.96-4.16) close to those for band B of nitrobenzene in water solution (267 mμ, $\lg \epsilon$ 3.91) [7].

As in nitrobenzene, in concentrated sulfuric acid the edge of the long wave shoulder of the absorption curve of the nitrobenzoic acids and their esters remains at the same wavelength as in dioxane, but the bands are shifted markedly to the long wave side (Table 2), and in some of them (the meta-nitrobenzoic acid) they occupy almost the same position (λ 283 mμ and $\lg \epsilon$ 3.87) as in nitrobenzene (286 mμ, $\lg \epsilon$ 4.02). The appearance on the absorption curves of the nitrobenzoic acids and their esters of the bands of nitrobenzene occurs, however, only in those regions of the spectrum where the molecules absorb more intensely than the molecules of benzoic acid. In the short wave region in some of the compounds studied there appear bands of transfer of a charge characteristic for unsubstituted benzoic acid (in ethanol at 227 mμ and $\lg \epsilon$ 4.04, in cyclohexane at 230 mμ, $\lg \epsilon$ 4.13) [4, 12],

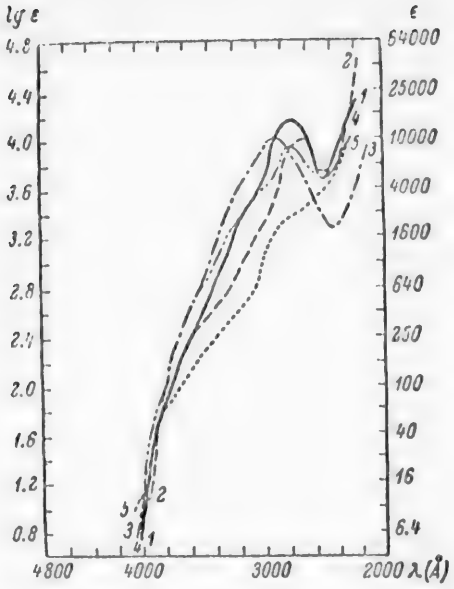

Fig. 1. Absorption curves. 1) o-Nitrobenzoic acid in 98% sulfuric acid, 2) o-nitrobenzoic acid in 9.8% sulfuric acid, 3) nitrobenzene in 98% sulfuric acid, 4) o-nitrobenzoic acid in 2 N alkali, 5) o-nitrobenzoic acid in dioxane.

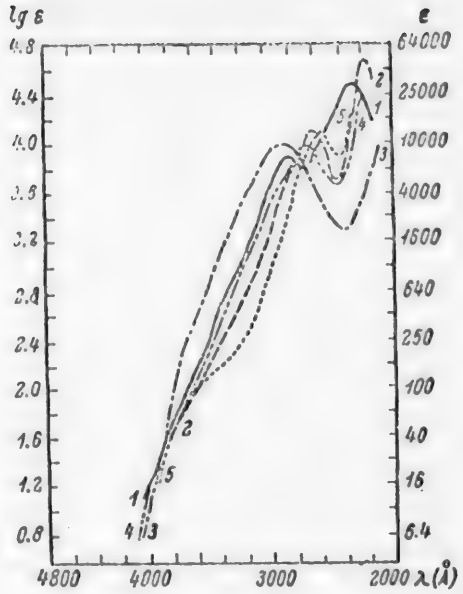

Fig. 2. Absorption curves. 1) m-Nitrobenzoic acid in 98% sulfuric acid, 2) m-nitrobenzoic acid in 9.8% sulfuric acid, 3) nitrobenzene in 98% sulfuric acid, 4) m-nitrobenzoic acid in 2 N alkali, 5) m-nitrobenzoic acid in dioxane.

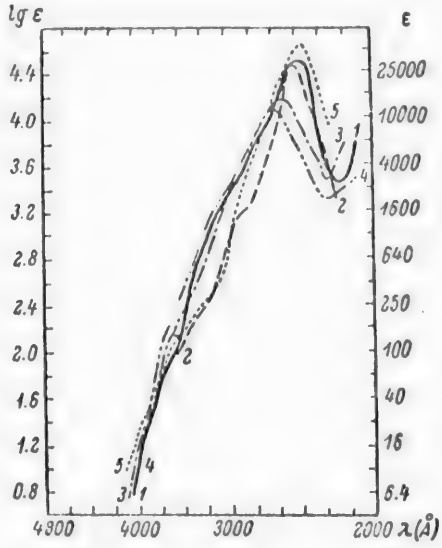

Fig. 3. Absorption curves. 1) p-Nitrobenzoic acid in 98% sulfuric acid, 2) p-nitrobenzoic acid in 9.8% sulfuric acid, 3) p-nitrobenzoic acid in 2 N alkali, 4) nitrobenzene in 98% sulfuric acid, 5) p-nitrobenzoic acid in dioxane.

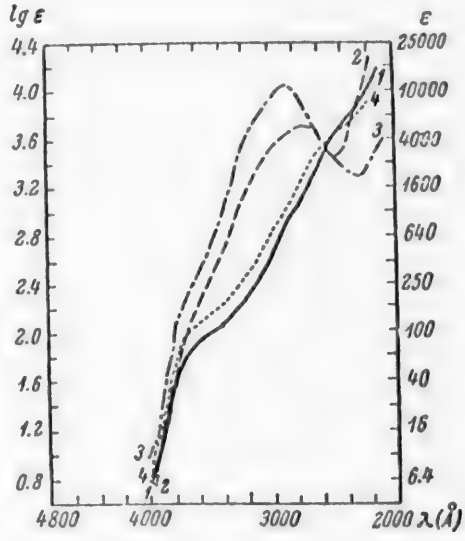

Fig. 4. Absorption spectra of ethyl o-nitrobenzoates. 1) In hexane, 2) in 98% sulfuric acid, 3) in butanol, 4) nitrobenzene in 98% sulfuric acid.

TABLE 1

Characteristics of Absorption Curves for Compounds of the Composition $NO_2C_6H_4COOR$

R	Isomer	Solvent	Long wave shoulder		Band (shoulders)					
					$A_{1g} \rightarrow B_{2u}$		$^{B}C_6H_5NO_2$		$^{B}C_6H_5COOR$	
			~λ(mμ)	lg ε	λ (mμ)	lg ε	λ (mμ)	lg ε	λ (mμ)	lg ε
H	o-	Benzene	332	2.60	–	–	–	–	–	–
		Dioxane	330	2.50	–	–	~250	3.60	228	4.02
		Ether	327	2.52	–	–	–	–	226	4.20
		Butanol	322	2.70	–	–	–	–	–	–
		NaOH	–	–	~295	3.64	273	3.96	–	–
		Concentrated H_2SO_4	–	–	~296	3.70	274	4.16	–	–
		Dilute H_2SO_4	342	2.30	–	–	265	4.00	–	–
H	m-	Benzene	336	2.30	–	–	–	–	–	–
		Dioxane	346	2.13	–	–	254	4.10	–	–
		Ether	323	2.34	–	–	260	4.27	–	–
		Butanol	322	2.33	–	–	255	3.97	–	–
		NaOH	355	2.20	–	–	270	3.97	–	–
		Concentrated H_2SO_4	352	2.30	–	–	283	3.87	231	4.48
		Dilute H_2SO_4	–	–	–	–	263	4.10	222	4.68
H	p-	Dioxane	354	2.25	–	–	256	4.62	–	–
		Ether	360	2.10	–	–	265	4.33	–	–
		Butanol	338	2.70	–	–	253	4.30	–	–
		NaOH	362	2.30	–	–	273	4.16	–	–
		Concentrated H_2SO_4	360	2.20	–	–	260	4.50	–	–
		Dilute H_2SO_4	336	2.46	~300	3.30	263	4.46	–	–
C_2H_5	o-	Hexane	339	2.07	–	–	~242	3.70	–	–
		Benzene	310	2.70	–	–	–	–	–	–
		Dioxane	320	2.52	–	–	~254	3.60	–	–
		Ether	339	2.22	–	–	~255	3.70	–	–
		Butanol	340	2.25	–	–	~254	3.60	–	–
		Concentrated H_2SO_4	–	–	–	–	273	3.72	–	–
C_2H_5	m-	Hexane	310	2.00	~280	3.05	251	3.90	–	–
		Benzene	332	2.10	–	–	–	–	–	–
		Dioxane	328	2.05	–	–	~258	3.70	–	–
		Ether	330	2.10	–	–	255	4.01	–	–
		Butanol	325	2.08	–	–	~248	3.80	–	–
		Concentrated H_2SO_4	350	2.08	–	–	~260	3.80	–	–
C_2H_5	p-	Hexane	–	–	~290	3.20	255	4.28	–	–
		Benzene	346	2.10	–	–	–	–	–	–
		Dioxane	335	2.30	–	–	260	4.01	–	–
		Ether	328	2.60	–	–	256	4.48	–	–
		Butanol	345	2.10	–	–	253	4.08	–	–
		Concentrated H_2SO_4	–	–	~315	3.20	267	4.16	–	–

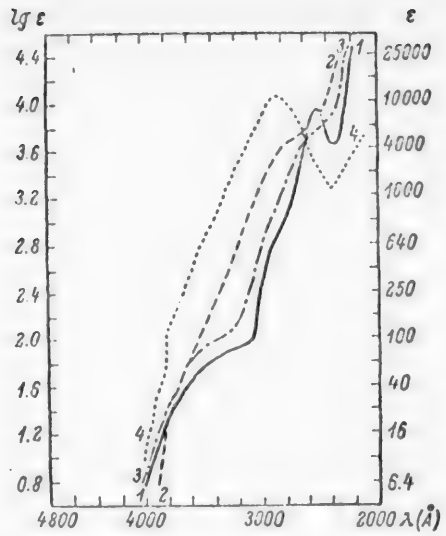

Fig. 5. Absorption spectra of ethyl m-nitrobenzoate. 1) In hexane, 2) in 98% sulfuric acid, 3) in butanol, 4) nitrobenzene in 98% sulfuric acid.

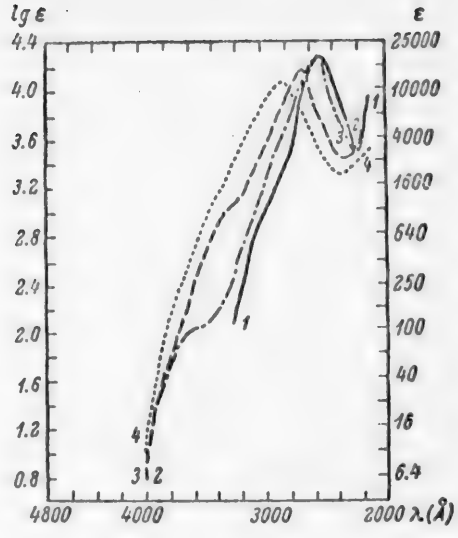

Fig. 6. Absorption spectra of ethyl p-nitrobenzoate. 1) In hexane, 2) in 98% sulfuric acid, 3) in butanol, 4) nitrobenzene in 98% sulfuric acid.

TABLE 2

Relation of the Characteristics of the Bands in Disubstituted Compounds $NO_2C_6H_4COR$ in Hexane (dioxane for acids)

R	Isomer	E_{max} (in eV)	$\Delta E = E_{NO_2,\ COR} - E_{NO_2}$ (in eV)	$\frac{\varepsilon_{NO_2,\ COR}}{\varepsilon_{NO_2}}$	$\Delta E = E_{hexane\ (dioxane)} - E_{conc.\ H_2SO_4}$
OH	o-	~4.90	~+0.03	~0.5	~+0.47
	m-	4.81	−0.06	1.2	+0.49
	p-	4.78	−0.09	4.0	+0.08
OC_2H_5	o-	~5.05	~+0.18	~0.5	~+0.57
	m-	4.87	0.00	0.81	+0.17
	p-	4.80	−0.07	1.9	+0.32
H	o-	~4.97	~+0.10	~1.0	~+0.66
	m-	~4.83	~−0.04	~1.0	~+0.32
	p-	4.67	−0.20	3.1	+0.29
CH_3	o-	~5.10	~+0.23	~0.75	~+0.66
	m-	~4.90	~+0.03	~0.95	~+0.43
	p-	4.74	−0.13	2.5	+0.49

and in concentrated sulfuric acid in some of the nitro compounds studied the bands are found at the same values of wavelength and extinction as in benzoic acid in this medium (λ 260 mμ, lg ε 4.19) [4], and in others at intermediate values for this acid and nitrobenzene. Evidently the absorption curves of these disubstituted compounds with the composition AC_6H_4A' consist of curves superimposed on each other from the constituting monosubstituted substances C_6H_5A and C_6H_5A', and in the separate parts the curves of the compounds predominate which absorb more strongly in that region.

The presence of a carboxyl or carboxyethyl group also produces some difference in the position of the band $B_{C_6H_5NO_2}$ in the different isomers. As Table 2 shows, band B in these and in other compounds of the same type [1] is shifted toward the long wave side in the isomers with increasing intensity in the order p- > m- > o-. Here in

the ortho isomer as compared to the position in the unsubstituted nitrobenzene there is somewhat of a shift toward the short waves with a marked fall in intensity, and in the para isomer, on the contrary, toward the long waves with a sharp increase in extinction and oscillation strength; in the meta isomer, as a rule, it occupies almost the same position as in the nitrobenzene. By this and also by the superposition of the long wave edge of the band $B_{C_6H_5COR}$ or the band of the $A_{1g} \rightarrow B_{1u}$ transfer we can explain why in the ortho isomer (and sometimes in the meta isomer) the band $B_{C_6H_5NO_2}$ appears only in the form of a shoulder. The decreased extinction of band B of the ortho isomer in this type of compound can be explained by the steric effect which draws the nitro group from the plane of the ring [8, 13, 14]. As the data of Table 2 show this steric effect appears not only in the decreased extinction [8, 14, 15] but also in the hypsochromic shift of the band. As evidence for the presence of this effect we also find it to increase in going from the acids to the esters.

It also follows from our results that in these compounds the "indirect" steric effect assumed in the meta isomer [16] is actually absent; the idea of such an effect was evidently suggested by the unjustified comparison of the intensity of band B not with such nitrobenzenes, but with the corresponding para isomers, and with data for ethanol (where specific effects of the solvent can be superimposed) and not for hydrocarbon solvents.

Some shift of band B of the para isomer toward the longer waves (Table 2) cannot be explained only by a difference in inductive effect of the functional groups in the ground and excited states, since in this case we would expect a greater bathochromic shift in the meta isomer than in the para isomer. Competing groups as centers of negative charge in the excited state [14, 17] not only cannot explain the difference in behavior of the para and meta isomers in this type of compound but also such a great increase in intensity and oscillation strength of this band of the para isomer. There remains only the suggestion that in the excited state the less active group (in this case COR) changes its usual effect which it has in the ground state and becomes an electron donor group, shifting to some extent its π-electron in the ring [18], which will permit not only the observed shift of the band, but also the great increase in excitation of the dipole moment of the molecule and hence the intensity of absorption.

SUMMARY

1. On the basis of results of measurement of absorption of o-, m-, and p-nitrobenzoic acids and ethyl benzoates in seven different solvents it is shown that the absorption curves of compounds with the composition AC_6H_4A (where A is an electron accepting group) consist of the curves of the corresponding monosubstituted derivatives superimposed on each other with predominance in different parts of the curve of the compound which absorbs more actively in that portion.

2. In the excited state, the less active group of this type of compound can change its electrical effect by shifting electrons and from an electron acceptor become an electron donor.

3. The steric effect in the ortho isomer of the disubstituted compound AC_6H_4A causes not only a lessening of intensity of band B, but also shifts it toward the short waves.

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STUDIES IN THE CYCLOBUTANEDICARBOXYLIC ACID SERIES

III. BASIC ESTERS OF α-TRUXILLIC ACID

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There are described in the literature only a few examples of basic esters of diphenylcyclobutane dicarboxylic acids. These include the α- and β-truxilline-like alkaloids of the cocaine group, which are tropine esters of α-truxillic and β-truxillic acids [1]; there is also information [2] on the interesting pharmacological properties of the alkaloid thesine, the di-d-isoretronecanol ester of p, p'-dihydroxy- α-truxillic acid [3].

Derivatives of the stereoisomeric 1,3-diphenylcyclobutane-2,4-dicarboxylic acids can serve as suitable objects for studying some questions of the relation of biological activity to spatial factors. In the present communication we describe a series of dialkylaminoalkanol esters of α-truxillic acid (I) obtained for a comparative pharmacological study.

Esters of (I) were obtained by reaction of four moles of α,ω-dialkylaminoalkanols $HO(CH_2)_nNR'R''$ (II) with one mole of α-truxillic acid dichloride in benzene solution; after separation of the precipitated hydrochloride• the basic ester remained as a thick mass which could not in all cases be induced to crystallize. The esters (I) were characterized by conversion to the dimethiodides•• and in some cases to the dihydrochlorides. The typical experimental conditions are given in the experimental part for (I) (n = 4, R' and R'' = $(CH_2)_5$; the properties and results of analysis of the compounds obtained are given in the Table.

For comparative study of the pharmacological action of the reesterification of dimethyl esters of cis-1,3-cyclobutane dicarboxylic acid with β-dimethylaminoethanol we obtained the di-β-dimethylaminoethyl ester of cis-1,3-cyclobutane dicarboxylic acid.

Pharmacological study of the synthesized preparations••• showed that some of the dimethiodides had high curare-like activity with short duration of action: the most interesting from this point of view was the compound with n = 4.

EXPERIMENTAL

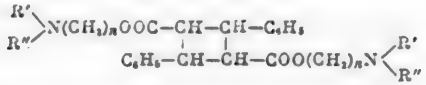
Di-4-N-piperidylbutanol ester of α-truxillic acid. To a solution of 9.6 g of 4-N-piperidylbutanol in 50 ml of benzene cooled to 0° was added dropwise a solution of 5.2 g of α-truxillic acid dichloride in 50 ml of benzene, after which the reaction mixture was heated for four hours with boiling of the benzene. After cooling, the 4-N-piperidylbutanol hydrochloride which precipitated was filtered off and washed with benzene. The benzene was

• In the case of (II) (n = 2, R' = R'' = CH_3) the hydrochloride of ester (I) (n = 2, R' = R'' = CH_3) precipitated from the reaction mixture.

•• The dimethiodides of esters which contained the heptanol chain with n = 7 were very slightly soluble in water and organic solvents.

••• Carried out by D. A. Kharkevich and L. A. Kravchuk in the laboratory of a separate pharmacological institute.

Dialkylaminoalkyl Esters of α-Truxillic Acid



R′	R″	n	Empirical formula	M.p. (from ligroin)	Base						Methiodide		
					yield, %	found, %[a]			calculated, %			m.p.	% I	
						C	H	N	C	H	N		found	calculated
CH_3	CH_3	2	$C_{26}H_{34}O_4N_2$ [b]	52—53	92	71.79	8.07	6.28	71.23	7.76	6.39	280° (decomp.)	35.32	35.18
C_2H_5	C_2H_5	2	$C_{30}H_{42}O_4N_2$		71	71.84	8.63	5.99	72.05	8.50	5.71	205—206	32.58	32.60
CH_3	CH_3	3	$C_{28}H_{38}O_4N_2$ [c]	79 (from ether)	69	71.87	8.10	6.10	72.20	8.15	6.00	230—232	34.33	33.86
C_2H_5	C_2H_5	4	$C_{34}H_{50}O_4N_2$ [d]		83	73.55	9.57	6.07	74.18	9.09	5.90	141.5	30.20	29.48
$-(CH_2)_5-$		4	$C_{36}H_{50}O_4N_2$	56—57	79	75.55	8.85	5.01	75.48	8.79	4.88	228	29.70	29.60
$-(CH_2)_2O(CH_2)_2-$		4	$C_{34}H_{46}O_6N_2$	69—70	60	70.92	8.20	4.70	70.65	8.02	4.83	218	29.70	29.46
C_2H_5	C_2H_5	7	$C_{40}H_{62}O_4N_2$		91	74.95	10.23	4.73	75.71	9.85	4.41	187—188	e	
$-(CH_2)_5-$		7			60							201—202	f	

[a] We give average values for two determinations.

[b] Dihydrochloride: m.p. 243°. Found %: Cl 13.81. $C_{26}H_{34}O_4N_2 \cdot 2HCl$. Calculated %: Cl 13.89.

[c] Dihydrochloride: m.p. 186°. Found %: Cl 12.79. $C_{28}H_{38}O_4N_2 \cdot 2HCl$. Calculated %: Cl 13.18.

[d] The substance was isolated as the dihydrochloride, m.p. 149°. Found %: Cl 11.26. $C_{34}H_{50}O_4N_2 \cdot 2HCl$. Calculated %: Cl 11.39.

[e] Found %: C 54.44; H 7.78. $C_{40}H_{62}O_4N_2 \cdot 2CH_3I$. Calculated %: C 54.90, H 7.42.

[f] Found %: C 56.00; H 7.41. $C_{42}H_{62}O_4N_2 \cdot 2CH_3I$. Calculated %: C 56.04, H 7.22.

distilled from the combined filtrates in a vacuum and the residue was dissolved in 1 N hydrochloric acid, extracted with ether, the water layer was made alkaline with a concentrated solution of ammonia, and the precipitated base was extracted with ether. After removal of the ether we obtained 7 g (77%) of an oily yellow residue which crystallized only after long standing: m.p. 56-57°.

Dimethiodide. A solution of 2 g of base and 4 g of methyl iodide in 20 ml of methanol was heated to boiling for two hours and the crystals which separated on cooling were recrystallized from methanol. Yield 2 g, m.p. 228°. The substance was difficultly soluble in water and methanol.

Di-β-diethylaminoethyl ester of cis-1,3-cyclobutanedicarboxylic acid. To 12 g of β-diethylaminoethanol was added about 0.1 g of metallic sodium and after solution of the latter we added 6 g of the dimethyl ester of cis-1,3-cyclobutane dicarboxylic acid [4]. The mixture was heated for five hours on a boiling water bath with a reflux condenser at a residual pressure of 40-60 mm, the excess diethylaminoethanol was distilled off in a vacuum, the residue was mixed with 20 ml of water, hydrochloric acid was added to an acid reaction, and it was extracted with ether. The aqueous solution was made alkaline with sodium hydroxide and extracted with ether; the residue after removal of the solvent was distilled in a vacuum. We obtained 6.8 g of a substance with b.p. 173-176° (3 mm), nD^{20} 1.4601.

Found %: C 62.82, 62.94; H 10.32, 10.20; N 8.11, 8.01. $C_{18}H_{34}O_4N_2$. Calculated %: C 63.18; H 9.94; N 8.18.

Dimethiodide. A mixture of 2 g of the base, 3 g of methyl iodide, and 10 ml of methanol was heated two hours under reflux. The residue after distillation of the methanol was dissolved in water, extracted with ether, and the water layer was evaporated in a vacuum. We obtained 3.6 g of a glassy, noncrystalline mass, easily soluble in water and alcohol, difficultly soluble in ether and acetone.

Found %: I 39.87. $C_{18}H_{34}O_4N_2 \cdot 2CH_3I$. Calculated %: I 40.56.

SUMMARY

We have obtained a series of dialkylaminoalkyl esters of α-truxillic acid for comparative pharmacological study.

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THE CATALYTIC CONDENSATION OF SCHIFF BASES WITH ORGANIC SUBSTANCES

III. THE MECHANISM OF THE SYNTHESIS OF β-ARYLAMINOKETONES

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In our previous communications [1, 2] we described a process of obtaining β-arylaminoketones by condensation of Schiff bases with alkylaromatic ketones in the presence of amine hydrochlorides as catalysts, salts which entered the composition of the bases: the alkylaromatic ketones added to the Schiff bases at the azomethine bond which, as is known, tends to be polarized.

$$RC_6H_4N{=}CHC_6H_5 \xrightarrow{CH_3COC_6H_5} RC_6H_4NH{-}\underset{\displaystyle CH_2COC_6H_5}{\underset{|}{CH}}{-}C_6H_5 \quad (I)$$

It was then noticed that the β-arylamino-β-phenylpropiophenones which we synthesized, in an acid medium easily split into the primary amine and chalcone. At the same time a method was described in the literature for obtaining β-arylaminoketones by condensation of primary aromatic amines with chalcones in an alkaline medium [3].

In the present work we decided to study this reaction in the presence of our suggested acid catalysts. In this reaction we used aniline, m- and p-toluidine, p-anisidine, m- and p-nitroaniline, and 2-naphthylamine, and for the chalcones: benzalacetophenone; the catalyst was the hydrochloride of the amines used. As the final product of the reaction we obtained the corresponding β-arylaminoketones; hence the aromatic amines add to the chalcone at the double bond.

$$RC_6H_4NH_2 \xrightarrow{C_6H_5CH{=}CHCOC_6H_5} RC_6H_4NH{-}\underset{\displaystyle CH_2COC_6H_5}{\underset{|}{CH}}{-}C_6H_5 \quad (II)$$

In the final account, in both methods for the synthesis of β-arylaminoketones the starting products are the same, the primary aromatic amine, aromatic aldehyde, and alkylaromatic ketone, but they enter the reaction in a different order. Thus, in the first method the primary aromatic amine first reacts with the aromatic aldehyde and the resulting Schiff base reacts with the ketone. In the second method the aromatic aldehyde first reacts with the ketone, and the resulting chalcone reacts with the primary aromatic amine. Hence, the Schiff base and the chalcone are intermediate products in the synthesis of β-arylaminoketones.

However, it is known from the literature that both chalcones [4] and Schiff bases [5] undergo hydrolytic splitting. Hence, the question naturally arises, are the above reactions (I),(II) independent, or does the synthesis of

Starting amine	Synthesized β-aminoketone	M.p.	Yield, %
aniline	β-(anilino)-β-phenylpropiophenone	170°	52.4
p-toluidine	β-(p-toluidino)-β-phenylpropiophenone	171	42.2
m-toluidine	β-(m-toluidino)-β-phenylpropiophenone	134	44
p-anisidine	β-(p-anisidino)-β-phenylpropiophenone	148	41
m-nitroaniline	β-(m-nitroanilino)-β-phenylpropiophenone	145	27
p-nitroaniline	β-(p-nitroanilino)-β-phenylpropiophenone	184	34
2-Naphthylamine	β-(2-naphthylamino)-β-phenylpropiophenone	199	55

β-arylaminoketones proceed by one mechanism. In the first case we would expect that the Schiff base added to the reaction would be first hydrolyzed and the resulting aromatic aldehyde would react with the ketone, giving the chalcone, which would react with the primary amine (III).

$$ArN{=}CHR \xrightarrow{H_2O} ArNH_2 + RCHO$$

$$RCHO \xrightarrow[-H_2O]{CH_2COR'} RCH{=}CHCOR' \xrightarrow{ArNH_2} ArNH{-}\underset{\displaystyle CH_2COR'}{\underset{|}{CH}}{-}R \qquad (III)$$

In the second case we could have hydrolysis of the chalcone to ketone and aromatic aldehyde; the latter, reacting with the aromatic amine, would form the Schiff base, which with the ketone would give the β-arylaminoketone.

To settle this question of whether under our conditions there was hydrolysis of the Schiff base or the chalcone in the starting product, we heated the chalcone in aqueous alcohol with aniline hydrochloride and showed that the chalcone remained unchanged and so reaction (II) had independent significance. Experiments on condensation of Schiff bases with acetophenone and salts of aromatic amines in dry benzene led to the synthesis of β-arylaminoketones; this shows that reaction (I) can have independent significance.

We have established that reactions (I and II) are also determined by the properties of the Schiff base and chalcone; thus, in experiments on condensation of m- and p-nitrobenzalaniline with acetophenone in alcohol solution in the presence of aniline hydrochloride the chief reaction product was the m- or p-nitrochalcone. Hence, in the condensation of a Schiff base with an alkylaromatic ketone in aqueous alcohol in the presence of an acid catalyst the possibility is not excluded that there is hydrolysis of the Schiff base and formation of the chalcone.

We have also established that the direction of reaction (II) is also determined by the properties of the chalcone. Thus, attempts to introduce m- and p-nitrochalcones into reaction with aniline and m- and p-toluidine did not succeed. Hence, the greater the ability of the Schiff base to be hydrolyzed, the greater the affinity of the amine for the chalcone, the greater will be the probability that the first process of synthesis of the β-arylaminoketones will occur by mechanism (III).

EXPERIMENTAL

Method of synthesis of β-arylaminoketones. The reaction mass from the primary aromatic amine (0.02 g mole), chalcone (0.02 g-mole), 5-10 ml of alcohol, and 1 g of hydrochloride of the amine used was heated in a sealed glass tube for 0.5-1.0 hour on a boiling water bath. The tube was cooled in the refrigerator, the crystals were separated, treated with aqueous ammonia to an alkaline reaction, and crystallized from alcohol or benzene. The resulting β-arylaminoketones are shown in the Table.

The structures of the substances obtained were shown by mixed melting points with their corresponding commercial known β-arylaminoketones, they showed no depression of the melting point. If under the same conditions in the reaction with aniline, m-, or p-toluidines, we used m- and p-nitrochalcones, formation of the corresponding β-arylaminoketones did not occur; the starting substances remained unchanged.

We showed in a special experiment that in the reaction of benzalaniline with acetophenone in dry benzene we obtained β-anilino-β-phenylpropiophenone with m.p. 172° in a yield of 46%.

SUMMARY

1. We have studied the reaction of catalytic condensation of primary aromatic amines with benzalacetophenone, as a result of which we obtained the corresponding β-arylamino-β-phenylpropiophenones.

2. We have discussed the mechanism of the reaction of synthesis of β-arylamino-β-phenylpropiophenones starting from the Schiff bases and ketones and from primary aromatic amines and chalcones.

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THE REPLACEMENT OF HALOGENS IN AZO COMPOUNDS

XL THE SIGNIFICANCE OF SOME SPATIAL FACTORS

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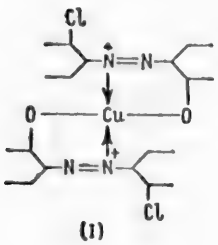
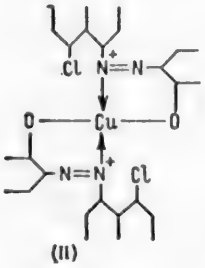
The question of the reasons for the unusual ease (for aromatic compounds) of the replacement of halogen atoms in o-halogeno-o'-hydroxyazo compounds in the presence of copper salts [1-5] still remains unsettled. Since we have established that the replacement of halogen occurs with the same ease in the absence of free Cu salts [6] in copper complexes of o-halogeno-o'-hydroxyazo compounds, we have suggested [7] that the weakening of the bond of the halogen atom with the carbon of the aromatic ring is due to the occurrence in complex formation of a positive charge on the nitrogen atom of the azo group which is located in the ortho position to the halogen atom (I).



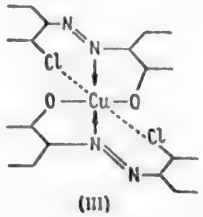
(I)



(II)

This suggestion, however, fails when it is found that on the one hand, the halogen atoms in p-halogeno-o'-hydroxyazo compounds are not substituted under analogous conditions [8] although they are submitted to practically the same effects from the positively charged nitrogen atom of the azo group, and on the other, that the halogen atoms in peri-halogen-o'-hydroxyazo compounds and their copper complexes (II) have almost the same mobility as in the o-halogeno-o'-hydroxyazo compounds; here the effect of the nitrogen charge on the bond of halogen with carbon in the peri position cannot occur [7, 9].

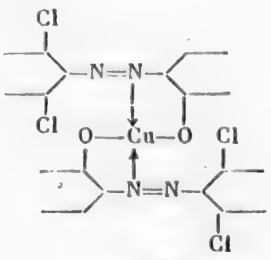
The assumption remains that the reason for the weakening of the halogen-carbon bond in the aromatic ring in compounds of this type is some sort of reaction between these and the metal atom in the intermediate formation of the complex (III).



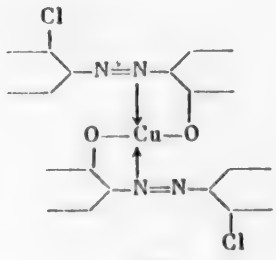
(III)

At the present time we do not have the data for judging the nature of this reaction. It is not impossible that this is the ordinary coordination bond formed because of one of the unshared electron pairs of the halogen atom. It is necessary to note that such a reaction of halogen with the metal atom is possible from steric considerations only under conditions of formation of a five-membered ring (III) and not a six-membered one (I, II), that is, with participation in the complex formation of a nitrogen atom of the azo group connected with the aromatic nucleus which carries the hydroxy group, but not the halogen atom.

If the suggestion of reaction in the complex of an atom of copper with an atom of halogen as the reason for the mobility of the latter is correct, then we should expect that when two atoms of halogen are present in the ortho position to the nitro group, in o, o-dihalogeno-o'-hydroxyazo compounds, their substitution should occur more easily than the single halogen atom in o-halogeno-o'-hydroxyazo compounds. In fact, in the first case, at any rotation of the aromatic ring around the C-N bond one of the halogen atoms is found in the complex close to the copper atom (IV), while in the second case, besides complex (III), complex (V) can also form with an unfavorable arrangement of the halogen atoms.



(IV)

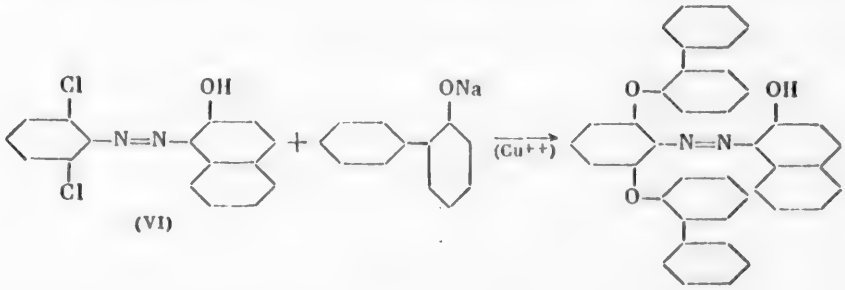


(V)

Since rotation around the C-N bond in this case is difficult due to reaction of the unshared electron pair of the nitrogen atom with the π-electrons of the aromatic ring, transformation of form (V) into form (III) requires the expenditure of energy. At the same time, replacement of the chloride atom in complex (IV) by groups which have a considerable size causes spatial difficulties which cause rotation around the C-N bond, evidently without further expenditure of energy; as a result the remaining halogen atom approaches the copper atom and by reacting with it acquires the ability to be replaced.

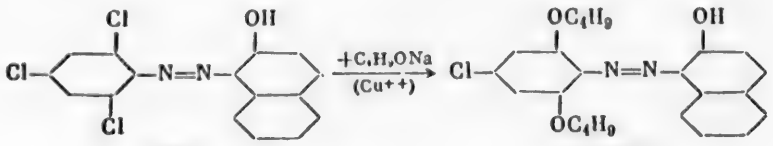
Actually we have shown [10] that in the reaction of 2,6-dichlorobenzene(1-azo-1')-2'-naphthol [azo dye (VI) from 2,6-dichloroaniline and 2-naphthol] with sodium n-butylate and 4-phenylphenolate in the presence of copper acetate there occurs quantitative replacement of both chlorine atoms by the corresponding alkoxy or aryloxy groups and this reaction occurs considerably more easily than in the replacement of a single atom of chlorine in 2-chlorobenzene(1-azo-1')-2'-naphthol (the dye from 2-chloroaniline and 2-naphthol). In particular, in the reaction of the dye from 2,6-dichloroaniline with sodium n-butylate the replacement of both chlorine atoms occurs quantitatively in 30 minutes at 100° while in the dye from 2-chloroaniline the quantitative replacement of one atom of chlorine under the same conditions takes two hours.

Continuing work in this direction, we have studied the reaction of 2,6-dichlorobenzene(1-azo-1')-2'-naphthol (VI) with sodium 2-phenylphenolate and of 2,4,6-trichlorobenzene(1-azo-1')-2'-naphthol [dye (VII), from 2,4,6-trichloroaniline and 2-naphthol] with sodium n-butylate, in both cases in the presence of copper acetate. In the first case with heating for four hours at 100° both atoms of chlorine are quantitatively replaced by the 2-phenylphenoxy group.



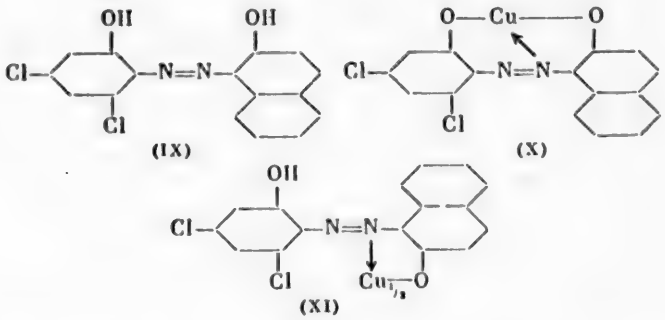
(VI)

In the second case with heating 30 minutes at 50° about 63% of the chlorine contained in the starting trichloroazo compound is split out, which corresponds to an almost quantitative (about 95.5%) replacement of two chlorine atoms. Increase in reaction time to 2 hours did not cause an increased amount of splitting of chlorine. We isolated from the reaction mass in a yield of about 94% a reaction product which contained, according to the results of elementary analysis one atom of chlorine and two butoxy groups. We did not make a special study of the position of the chlorine atom; however, considering on the one hand the ease of replacing the halogen atoms in such compounds in the ortho position to the azo group [10], and on the other the absence of replacement of halogens in the para position to the azo group [8], we consider that the compound which we have obtained is 4-chloro-2,6-dibutoxybenzene(1-azo-1')-2'-naphthol (VIII), that is, the reaction occurs according to the scheme:



(VII) (VIII)

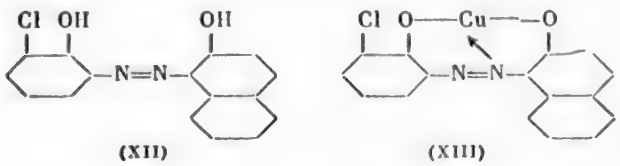
Further confirmation of the role of spatial approach of halogen atoms to the metal atom of the complex-former is seen in experiments on the reaction of 3,5-dichlorophenol(2-azo-1')-2'-naphthol [azo dye (IX) from 3,5-dichloro-2-aminophenol and 2-naphthol] with sodium n-butylate in the presence of copper acetate.



(IX) (X) (XI)

In this case the chlorine atom in the ortho position to the azo group, as in complex (XI), can react with the copper atom and gain a high mobility; in the case of formation of complex (X) the chlorine is spatially disconnected from the copper atom and should not be replaced by the butoxy group under mild conditions. It was shown that when heated eight hours at 100°, only 25% of the chlorine was split off of the amount present in the original dichloroazo compound. Increase in the period of heating to 20 hours did not change the result. Since the chlorine in the para position to the azo group does not react under these conditions [8], we must consider that this corresponds to the probability of formation of complex (XI).

As would be expected, 6-chlorophenol(2-azo-1')-2'-naphthol [azo dye (XII), from 6-chloro-2-aminophenol and 2-naphthol] in the complex (XIII), whose chlorine atom because of the great distance cannot react with the copper, remains unchanged when heated with sodium n-butylate in the presence of copper acetate for eight hours at 100°.



(XII) (XIII)

EXPERIMENTAL

Reaction of 2,6-dichlorobenzene(1-azo-1')-2'-naphthol (VI) with sodium 2-phenylphenolate. To a solution of sodium 2-phenylphenolate obtained by reaction of 0.51 g (0.003 g-mole) of 2-hydroxybiphenyl with 0.046 g (0.002 g-atom) of sodium in 15 ml of dioxane at 100° was added a mixture of a solution of 0.16 g (0.0005 g-mole) of 2,6-dichlorobenzene(1-azo-1')-2'-naphthol (m.p. 140-141° [10]) in 5 ml of dioxane and 0.05 g (0.00025 g-mole) of copper acetate in 10 ml of dioxane. The mass was heated with stirring for four hours at 100° after which 20 ml of 10% sulfuric acid was added. The tarry precipitate was filtered off and washed with distilled water. The filtrate and wash water were transferred to a calibrated flask, capacity 500 ml, and titrated potentiometrically (with silver and calomel electrodes, P-4 potentiometer) to determine the chlorine content. In the titration of two 10 ml samples we used on the average 2.005 ml of 0.01 N solution of silver nitrate, which corresponded to the presence in the reaction mass of 100.25% of the chlorine contained in the starting dichloroazo compound.

The precipitate was heated with 1% sodium hydroxide solution to remove the excess 2-hydroxybiphenyl, filtered, washed with water to a neutral reaction on brilliant yellow paper, and dried. Yield 0.31 g. A thick, viscous red mass. After standing two months, the mass crystallized; it was ground to a powder and recrystallized from a mixture of benzene and methyl alcohol (1:1). Yield 0.29 g (100%). Dark-red plates, m.p. 131-133.5°; chlorine absent (Beilstein test). 2,6-Di(2"-phenylphenoxy)benzene(1-azo-1')-2'-naphthol was easily soluble in benzene, toluene, dioxane, less so in acetone, poorly in methyl and ethyl alcohols.

Found %: C 82.35, 82.24; H 5.04, 5.06; N 5.05; 5.03. $C_{40}H_{28}O_3N_2$. Calculated %: C 82.17; H 4.83; N 4.79.

Reaction of 2,4,6-trichlorobenzene(1-azo-1')-2'-naphthol (VII) with sodium n-butylate. A mixture of solutions of 0.88 g (0.0025 g-mole) of 2,4,6-trichloro(1-azo-1')-2'-naphthol (m.p. 151.5-151.8° from a mixture of benzene with ethyl alcohol [11]) in 50 ml of toluene and 0.25 g (0.00125 g-mole) of copper acetate in 40 ml of n-butyl alcohol was added to a solution of sodium n-butylate heated to 50° (the butylate was prepared from 0.34 g (0.015 g-atom sodium with 10 ml of n-butyl alcohol) and the resulting mass was heated with stirring at 50°. After a definite time interval a 10 ml sample was taken and acidified with 5 ml of 10% sulfuric acid and washed with distilled water. The wash water was collected in a calibrated flask, capacity 50 ml, and the sample was titrated potentiometrically in 5 ml samples to determine the chlorine content in the reaction mass. Calculation of the amount of chlorine was carried out with respect to the content in the original trichloroazo compound. Results are given in Table 1.

TABLE 1

Kept at 50° (in hours)	No. ml of 0.01 N silver nitrate (av. of 2 samples)	Chlorine content in reaction mass, %
0.5	4.76	63.5
1.0	4.72	62.9
2.0	4.77	63.6

After keeping for two hours the reaction mass was acidified with 30 ml of 10% sulfuric acid, stirred 30 minutes, and washed free of acid with water. Toluene and butyl alcohol were distilled off in a vacuum to a final volume of about 3 ml. When the residue stood for two hours at 0° a precipitate came down which was filtered off, washed with methyl alcohol, and dried. Weight 0.88 g; after recrystallization from a mixture of methyl alcohol and benzene(2:1), fine needles with a cherry color, m.p. 92.7-93.5°. Easily soluble in benzene and toluene, poorly so in methyl and ethyl alcohols.

Found %: C 67.65, 67.81; H 6.59, 6.60; N 6.70; 6.81. $C_{28}H_{27}O_3N_2Cl$. Calculated %: C 67.51; H 6.37; N 6.56.

The filtrate after separation of the main precipitate was evaporated almost dry. We obtained 0.31 g of a tarry precipitate from which by crystallization from benzene we isolated 0.12 g of a substance which gave no melting point depression with the main product (m.p. 92.7-93.5°). Thus, in all we obtained 1.0 g (94.3%) of 4-chloro-2,6-dibutoxybenzene(1-azo-1')-2'-naphthol (VIII).

Reaction of 3,5-dichlorophenol(2-azo-1')-2'-naphthol (IX) with sodium n-butylate. To a solution of sodium n-butylate obtained from 0.08 g (0.003 g-atom) and 5 ml of n-butyl alcohol we added a mixture of solutions of 0.33 g (0.001 g-mole) of 3,5-dichloro(2-azo-1')-2'-naphthol (m.p. 218-218.5° from a mixture of benzene with alcohol, 5:1, see [12]) in 20 ml of toluene and 0.1 g (0.0005 g-mole) of copper acetate in 15 ml of n-butyl alcohol. The mass was heated with stirring for definite time intervals at 100°, after which it was acidified with 20 ml of 10% sulfuric acid and washed with distilled water. The wash water was collected in a calibrated flask, capacity 200 ml, and 10 ml samples were submitted to potentiometric titration with 0.01 N silver nitrate solution. Calculation of

TABLE 2

Kept at 100° (in hours)	ml 0.01 N silver nitrate (average of 2 samples)	Content of chlorine in reaction mass (in %) with respect to	
		total chlorine in original compound	one chlorine in original compound
8	2.53	25.25	50.5
20	2.28	22.75	45.5

the amount of chloride was carried out with respect to the chlorine contained in the starting dichloroazo compound and with respect to one atom of chlorine in this compound. The results of the determinations are given in Table 2.

Obtaining 6-chlorophenol(2-azo-1')-2'-naphthol (XII). 6-Chloro-2-nitrophenol was obtained by nitration of o-chlorophenol [13], m.p. 69.5-70.5° (cf. [14]). We dissolved 9.65 g of 6-chloro-2-nitrophenol at 90° in 200 ml of water and 5 ml of a solution of 40% sodium hydroxide. To the solution during 35 minutes we added 32 g of sodium hydrosulfite. The color then changed from dark red to light yellow. On cooling, a precipitate of white scales came down. Weight 1.82 g (23%). After recrystallization from dilute methyl alcohol (2 : 1), m.p. 80.5-81.5° (cf. [15]). We dissolved 1.93 g (0.0135 g-mole) of 6-chloro-2-aminophenol with heat in 30 ml of 10% hydrochloric acid, the solution was cooled to 0° and treated with 0.93 g (0.0135 g-mole) of sodium nitrite as a 10% solution. The resulting diazo solution was poured at 0° into a solution of 1.97 g (0.0135 g-mole) of 2-naphthol in a 10% solution of sodium hydroxide (0.54 g NaOH). For the coupling we added soda (about 1 g); the medium was always strongly alkaline to Brilliant Yellow paper. At the end of the addition of diazo solution the mass was stirred for two hours, then acidified with 10% hydrochloric acid and the dye was filtered, washed with water to the absence of acid to Congo paper, and air dried. Weight 2.87 g (70%). After recrystallization from a mixture of methyl alcohol and chlorobenzene (5 : 3), fine red-brown needles, m.p. 207.5-208.5°. 6-Chlorophenol(2-azo-1')-2'-naphthol was easily soluble in benzene, toluene, chlorobenzene, less so in methyl and ethyl alcohols.

Found %: N 8.94. $C_{16}H_{11}O_2N_2Cl$. Calculated %: N 9.37.

Reaction of 6-chlorophenol(2-azo-1')-2'-naphthol (XII) with sodium n-butylate. To a solution of sodium n-butylate obtained by reaction of 0.08 g (0.003 g-atom) of sodium with 5 ml of n-butyl alcohol we added a mixture of solutions of 0.3 g (0.001 g-mole) of 6-chlorophenol(2-azo-1')-2'-naphthol in 20 ml of toluene and 0.1 g (0.0005 g-mole) of copper acetate in 15 ml of n-butyl alcohol. The mass was heated for eight hours at 100°, then acidified with 20 ml of 10% sulfuric acid and washed with distilled water. Chlorine was determined in the wash water and was absent (test with silver nitrate). From the residue we separated a product which gave no melting point depression when mixed with the original dye (m.p. 207.5-208.5°).

SUMMARY

1. We have found that in the reaction of 2,6-dichlorobenzene(1-azo-1')-2'-naphthol with sodium 2-phenylphenolate in the presence of copper salts there is quantitative replacement of both atoms of chlorine by 2-phenylphenoxy groups.

2. We have found that in the reaction of 2,4,6-trichlorobenzene(1-azo-1')-2'-naphthol with sodium n-butylate in the presence of copper salts there is quantitative replacement of both chlorine atoms which are in the ortho position of the azo group by n-butoxy groups.

3. We have found that in the reaction of 3,5-dichlorophenol(2-azo-1')-2'-naphtholwith sodium n-butylate in the presence of copper salts there is replacement of 50% of the chlorine in the ortho position to the azo group.

4. We have considered the role of some spatial factors for the occurrence of the replacement of aromatically bound halogen atoms in azo compounds in the presence of copper salts. We have noted the significance of the possibility of a spatial approach of the halogen atoms to the copper atoms in the intermediate complex which is formed. We have suggested the reaction of the complex of metal atom-complex former and halogen as the reason for the weakening of the bond of the latter with the aromatic nucleus.

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SYNTHESIS OF 3-ISOPROPYL AND 3-PHENYLISOPROPYLSYDNONES AND THE CORRESPONDING SUBSTITUTED HYDRAZINES

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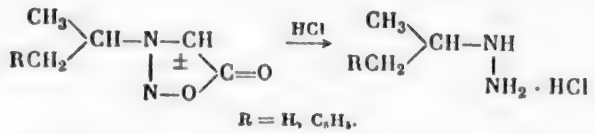
It was recently found that hydrazine derivatives and, in particular, phenylisopropylhydrazine and isonicotinic isopropylhydrazide (Marsilid) have a retarding effect on monoaminooxidase ferment.

As a result of our investigations on the synthesis and a study of the properties of the new and unusual heterocycles – sydnones [1] – containing the elements of hydrazine in the molecule and splitting up relatively easily, with the formation of the corresponding monosubstituted hydrazines [2], it was of interest to synthesize certain representatives of this class of compounds.

The present paper gives the synthesis of 3-isopropyl and 3-phenylisopropylsydnone, hitherto undescribed in the literature, and also isopropyl and phenylisopropylhydrazine hydrochloride, obtained by decomposition of these sydnones.



R = H, C_6H_5.

The ethyl ester of N-isopropyl glycine was synthesized by reacting isopropylamine obtained by reductive amination of acetone with the ethyl ester of bromoacetic acid. After it had been saponified with alkali, the acid was treated, without being separated, with sodium nitrite in acid. The precipitated N-nitroso derivative of N-isopropyl glycine was heated with excess acetic anhydride, as a result of which 3-isopropylsydnone was obtained. This compound is readily soluble in water and alcohol and insoluble in ether.

3-Phenylisopropylsydnone was synthesized in a similar way from phenylisopropylamine and the ethyl ester of chloroacetic acid. In this case, after saponification of the ester, phenylisopropyl glycine was precipitated as the hydrochloride and it was nitrosated. 3-Phenylisopropylsydnone was obtained from the nitroso derivative by the action of acetic anhydride. It is a high-boiling viscous liquid which must be distilled under high vacuum and in a current of nitrogen, otherwise it rapidly decomposes. Pure samples of sydnone gradually crystallize, forming a light-yellow oily powder practically insoluble in water. When the synthesized sydnones were heated with hydrochloric acid (1 : 1), isopropylhydrazine and phenylisopropylhydrazine hydrochlorides, corresponding to literature data, were obtained.

Since hydrazines with aliphatic and both aliphatic and aromatic substituents are not, in general, readily available, their synthesis via sydnones may be important.

EXPERIMENTAL

N-Nitroso-N-isopropylglycine. 68 g (0.49 mole) of the ethyl ester of bromoacetic acid was added with stirring to a solution of 48 g (0.33 mole) of isopropylamine in benzene. Heat was liberated. The mixture was boiled with stirring for 5 hours; it was cooled and the precipitated isopropylamine hydrobromide was filtered and washed with benzene. The benzene solution was evaporated under vacuum and the residue (64 g), the ethyl ester of N-isopropylglycine, was gradually added with stirring to a boiling solution of 25 g of caustic soda in 110 ml of water. The reaction mixture was boiled for 1 hour and was then cooled and twice extracted with ether. 100 ml of concentrated hydrochloric acid was added to an aqueous solution of the sodium salt of glycine and after the mixture had been cooled to 0° a solution of 43 g of sodium nitrite in 80 ml of water was gradually added with stirring. The reaction mixture was stired at the same temperature for 3 hours, and the precipitate was filtered and dried over alkali in a vacuum desiccator. A further amount of the nitroso derivative was obtained by extracting three times with ether. A total of 28 g was obtained; m.p. 131-132.5° (decomp., from water).

Found %: C 41.62; H 7.03; N 19.33. $C_5H_{10}O_3N_2$. Calculated %: C 41.09; H 6.89; N 19.17.

3-Isopropylsydnone. 26 g of the dried unrecrystallized N-nitroso-N-isopropylglycine was heated on a boiling water bath with 130 ml of acetic anhydride for 6 hours. After standing overnight, the acetic anhydride was distilled off under vacuum and the residue, in the form of a viscous oil, was crystallized. 16.5 g was obtained; m.p. 57-60° (from ether).

Found %: C 46.90; H 6.19; N 21.32. $C_5H_8O_2N_2$. Calculated %: C 46.56; H 6.29; N 21.86.

Isopropylhydrazine. 3.2 g of 3-isopropylsydnone was heated for 5 hours with 50 ml of hydrochloric acid (1 : 1) on a water bath, carbon dioxide being liberated. The solution was evaporated to dryness under vacuum, the residue (2.4 g) was dissolved in alcohol and 1.52 g (55.3 %) of isopropylhydrazine hydrochloride was obtained as a white, very hygroscopic powder (m.p. 112-114°) by precipitation with ether. Literature data [3]: m.p. 114°, 122-124°.

N-Phenylisopropylglycine hydrochloride. A mixture of 68 g (0.5 mole) of phenylisopropylamine and 30.6 g (0.25 mole) of chloroacetic ethyl ester was heated on a water bath for 5 hours. After the mixture had cooled, the phenylisopropylamine hydrochloride was filtered, the benzene was evaporated and the residue was washed with a solution of 18 g of caustic soda in 75 ml of water. The alkaline solution, washed with ether, was acidified with hydrochloric acid to pH 1-2. The precipitate was recrystallized in 10% hydrochloric acid. 31.2 g was obtained; the m.p. was 221-222° (decomp.).

Found %: Cl 15.63, 15.54. $C_{11}H_{15}O_2N \cdot HCl$. Calculated %: Cl 15.44.

N-Nitroso-N-phenylisopropylglycine. A solution of 10 g of sodium nitrite in 20 ml of water was added with cooling to 0-2° and stirring to a suspension of 29.3 g of N-phenylisopropylglycine hydrochloride in 180 ml of water. The mixture was stirred for 2 hours at this temperature; a viscous heavy oil separated out. The mixture was acidified with concentrated hydrochloric acid to pH 1-2; after the mixture had been allowed to stand, the oil crystallized out as a white powder, which was filtered, washed with water and dried over alkali in a desiccator. 19.5 g was obtained; the m.p. was 112-113° (from water).

Found %: C 59.27; H 6.29. $C_{11}H_{14}O_3N_2$. Calculated %: C 59.43; H 6.35.

3-Phenylisopropylsydnone. 19.5 g of N-nitroso-N-phenylisopropylglycine was mixed with 80 ml of acetic anhydride and after the mixture had stood at room temperature for 4 hours it was heated on a water bath. The acetic anhydride was removed at reduced pressure, and the residue was distilled in a current of nitrogen. 11.5 g was obtained; the b.p. was 204-205°(1.5 mm),194-196° (0.9 mm). It was a viscous yellow syrup, which crystallized out on standing; the m.p. was 45-46°.

Found %: C 65.01; H 6.11; N 13.89. $C_{11}H_{12}O_2N_2$. Calculated %: C 64.70; H 5.92; N 13.72.

Phenylisopropylhydrazine. 3 g of 3-phenylisopropylsydnone was heated on a water bath with 30 ml of hydrochloric acid (1 : 1) for 4 hours. The mixture was evaporated under vacuum and the residue was recrystallized from isobutyl alcohol. 1.67 g (60.5%) of phenylisopropylhydrazine hydrochloride was obtained; m.p. 118.5-119°. Literature data [4]: m.p. 122-124°.

SUMMARY

3-Isopropyl and 3-phenylisopropylsydnone were synthesized and 3-isopropyl and 3-phenylisopropylhydrazine hydrochloride were obtained from them.

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THE CATALYTIC ISOMERIZATION OF γ-OXIDES CONVERSION OF ALKYL TETRAHYDROFURYL CARBINOLS TO ALIPHATIC KETONES

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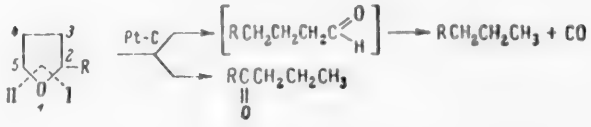
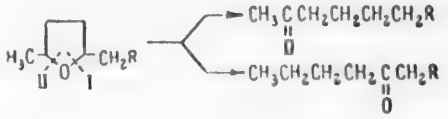
The catalytic isomerization of γ-oxides (tetrahydrofurans) to aliphatic carbonyl compounds in the presence of platinized charcoal is of great interest [1]. A detailed investigation of this reaction showed that unsymmetrical γ-oxides, for example α-alkyl tetrahydrofurans, isomerize in two directions.

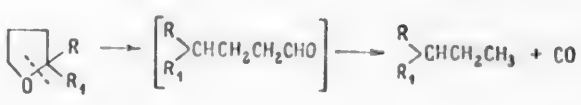


The length of the carbon chain of the alkyl radical located in the α-position and the reaction temperature have a very marked effect on the capacity of the γ-oxide ring to isomerize in one or another direction: with an increase in the reaction temperature and an increase in the length of side-chain alkyl group the capacity of the 1,2 C-O bond to undergo fission during isomerization of the ring increases while, on the other hand, this capacity decreases in the case of the 1,5 C-O bond [2].

The unequal tendency of the 1,2 and 1,5 C-O bonds to undergo fission during isomerization of a substituted tetrahydrofuran ring is also present in 2,5-dialkyl tetrahydrofurans, the alkyl groups of which contain a different number of carbon atoms. Isomerization of compounds of this type takes place primarily at the C-O bond in the vicinity of the longest alkyl radical [2].

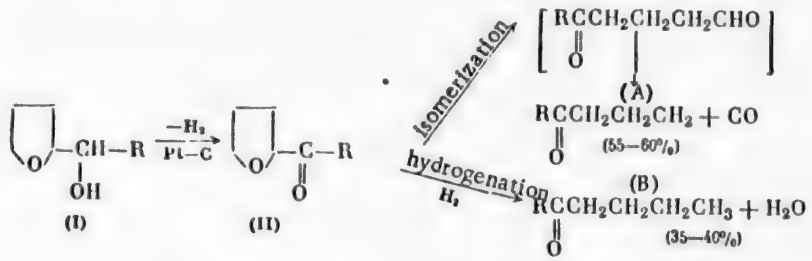


Finally, it should be mentioned that dialkyl tetrahydrofurans, both alkyl radicals of which are located on the same carbon atom of the ring in the α-position, isomerize with opening of the ring only at the C-O bond next to the side-chain alkyl groups; after decarbonylation of the intermediary aldehydes, this leads to the formation of the corresponding aliphatic hydrocarbons [2].



This report deals with an investigation of the catalytic isomerization of more complex representatives of γ-oxides, namely alkyl tetrahydrofuryl carbinols in the presence of platinized charcoal containing 10% platinum. It was to be expected that together with isomerization of the tetrahydrofuran ring, dehydrogenation of the alcohol to ketone, and certain other reactions associated with the presence of active hydrogen on the surface of a catalyst, would take place.

We carried out the isomerization of alkyl tetrahydrofuryl carbinols in the vapor phase at 280-300°. It was established that the principal reaction products are ketones (A) containing one carbon atom less in the molecule than the molecule of the initial alkyl tetrahydrofuryl carbinol. Ketones with this structure can only be formed as the result of opening of the tetrahydrofuran ring at the C-O bond next to the side-chain substituent, and decarbonylation of the intermediately formed ketoaldehyde to ketone (A). Together with this main direction of the reaction, conversions also take place, as a result of which aliphatic ketones (B) are formed, with the same number of carbon atoms as in the molecule of the initial alkyl tetrahydrofuryl carbinol.



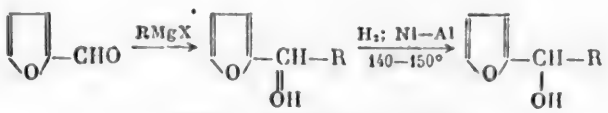
where R = CH_3; C_2H_5; iso-C_3H_7; n-C_4H_9.

The formation of ketones (B) is possible as a result of the hydrogenolysis of the ring in alkyl tetrahydrofuryl carbinols simultaneously at both C-O bonds by the hydrogen liberated during dehydrogenation of the carbinol, and also by the hydrogen adsorbed by the catalyst during reduction. Confirmation of this is provided by our experiments on the isomerization of alkyl tetrahydrofuryl carbinols in a current of hydrogen, which showed an appreciable relative increase in the yields of ketones (A) and a corresponding reduction in the yield of ketones (B); on the other hand, when the reaction was carried out as far as possible in absence of hydrogen (when the hydrogen adsorbed on the platinized charcoal was drawn off under vacuum at 300° for 6 hours), there was an increase in the yield of (B) ketones and a reduction in that of (A) ketones. It may be noted that there was always a small amount of α-diketones in the fractions containing the (B) ketones. Their formation is possible as a result of opening of the ring at the 1,5 C-O bond. The presence of α-diketones was indicated by the yellow-green color of the fractions, but it was impossible to isolate them in the pure form.

It is probable that the dehydrogenation of alcohol (I) to ketone (II) precedes the isomerization of the tetrahydrofurane ring. The preferential rupture of the latter at the 1,2 C-O bond would be explained in this case by the influence of the carbonyl group on the neighboring C-O bond in the ring. The presence of such an effect is indicated by the experimental data we obtained during the investigation of hydrogenation on platinum of furan compounds containing a carbonyl group in the vicinity of the ring [3].

EXPERIMENTAL

Synthesis of the initial substances. Alkyl tetrahydrofuryl carbinols were obtained according to the system:



= CH_3, C_2H_5, iso-C_3H_7, n-C_4H_9.

Properties of the Initial Alkyl Tetrahydrofuryl Carbinols

Name	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Literature
Methyl tetrahydrofuryl carbinol	92—93° (40)	1.0150	1.4485	[5]
Ethyl tetrahydrofuryl carbinol	62—63 (7)	0.9986	1.4497	[5]
Isopropyl tetrahydrofuryl carbinol	64—65 (8)	0.9901	1.4504	—
Butyl tetrahydrofuryl carbinol	97—98 (14)	0.9569	1.4508	[6]

The yields of alkyl furyl carbinols varied between 68 and 72% for ethyl and isopropylfuryl carbinols and 47-65% for methyl- and butylfuryl carbinols. Their catalytic hydrogenation was practically complete. The properties of the alkyl tetrahydrofuryl carbinols are given in the Table.

Catalyst. The catalyst, platinized charcoal, was prepared by impregnating activated birch charcoal with a solution of chloroplatinic acid, followed by reduction with formalin in alkali in the cold. It contained 10% finely dispersed platinum.

The isomerization of γ-oxides was carried out in the vapor phase at 280-300°. In each experiment we took 40-60 g of substances, which was passed through a layer of catalyst, with or without hydrogen, at a volumetric rate of 0.1 hour^{-1}. The dried catalyzates were distilled with an efficient column. The ketones obtained were characterized by the boiling point, the refractive index and the melting point of their semicarbazones. The properties of the ketones have been given previously [4].

SUMMARY

1. It was established that the γ-oxide ring in alkyl tetrahydrofuryl carbinols isomerizes in the vapor phase with platinized charcoal, the ring being opened at the 1,2 C-O bond next to the substituent in the α-position, the isomerization of the tetrahydrofuran ring evidently preceding the dehydrogenation of the alcohol to ketone. Decarbonylation of the intermediary ketoaldehydes gives aliphatic ketones with a chain having one carbon atom less.

2. Under the conditions employed, together with isomerization alkyl tetrahydrofuryl carbinols also undergo hydrogenation of the ring at both C-O bonds, with the formation of aliphatic ketones, the molecule of which contains the same number of carbon atoms as the molecule of the initial alkyl tetrahydrofuryl carbinols.

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A MODIFICATION OF THE DOEBNER-MILLER REACTION

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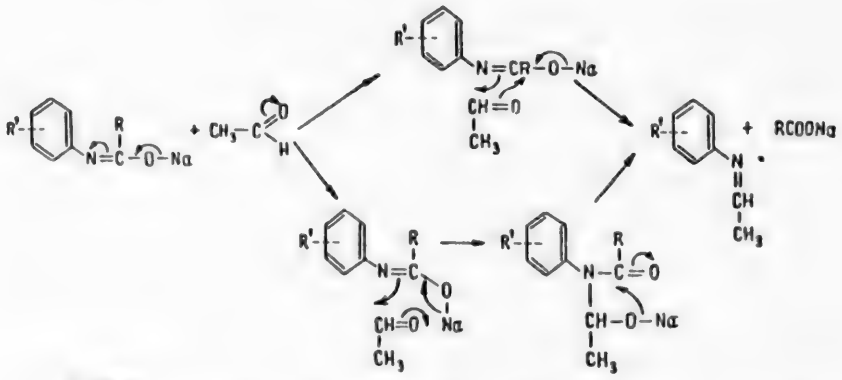
We previously proposed a new modification of the Doebner-Miller reaction with primary amines [1], the mechanism of which is mainly as follows. As was shown in the previous report, when acyl anilides react with sodium alcoholates in alcohol, and, in the case of formanilides, with alkali, a sodium derivative of acyl anilide is formed, which in its lactim form reacts with acetaldehyde.

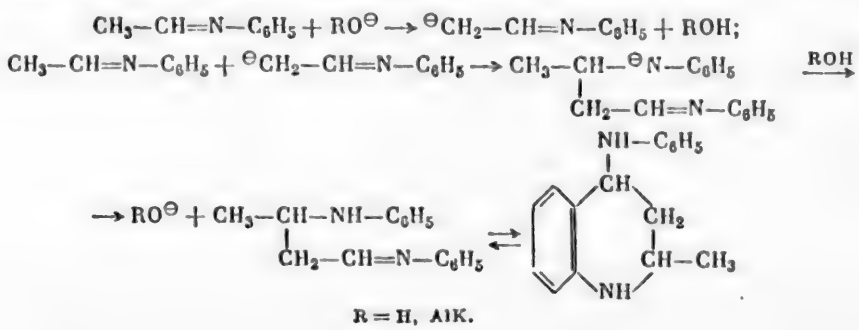


R = H, CH_3
R' = H, o-CH_3, m-CH_3, p-CH_3, o-OCH_3, p-OCH_3, o-OC_2H_5, p-OC_2H_5, o-Cl, p-Cl, etc.

The formation of ethylidene aniline may serve as an interesting example of the reactions of the conjugated system $-N=C-O-Me$ with transfer of the reaction center [2]. Whereas the silver derivative of formanilide

reacts withelectrophilic agents, for example alkyl iodides [3], without transfer of the reaction center (O reaction), the derivative of a less electronegative metal – sodium – can, according to A. N. Nesmeyanov, undergo a N reaction; in the given case the role of the electrophilic agent is played by acetaldehyde.

In the presence of such catalysts as alcoholate or hydroxyl anions the ethylidene aniline formed dimerizes to cyclic diethylidene diarylamines, according to the aldol system.



R = H, Alk.

Such products were isolated by E. I. Orlov [4] by reacting sodium formanilide with acetaldehyde, but he attributed the wrong structure to them.

If the second component of the aldol condensation is not ethylidene aniline but acetaldehyde, aldol bases are formed [5, 6] which are converted, however, to diethylidene diarylamines when heated with excess amine in acid [5]. Diethylidene diarylamines are converted to quinaldines according to the previously proposed systems [7, 8].

The present report describes quinaldine bases obtained from o-toluidine, m-toluidine and o-phenetidine with a yield of 30-35% relative to the initial amine, which is considerably higher than in the ordinary Doebner-Miller variant, where the yield does not exceed 13-15% [9, 10]. The reaction was also extended to chloroanilines. The use of caustic soda for obtaining sodium formanilides simplifies the synthesis and has hardly any effect on the yield of quinaldines.

EXPERIMENTAL

1. 8-Methylquinaldine. 100 ml of isobutyl alcohol and 2.3 g of sodium were placed in a twin-necked flask equipped with a reflux condenser, a mechanical stirrer and a dropping funnel. After the sodium had dissolved, 13.5 g of o-formotoluidide was added and 13.5 ml of paraldehyde was then added gradually for 15 minutes with heating. The mixture was boiled with stirring for 3 hours. When it had cooled, 40 ml of water and 40 ml of concentrated hydrochloric acid were added and the mixture was kept lightly boiling for another 2-3 hours, after which the alcohol was steam distilled. The residue was made alkaline and the base was also steam distilled. The mixture of amines was extracted with 80-100 ml of diethyl ether, shaken with 10 g of phthalic anhydride, and the phthalamic acids were extracted with a 10% solution of caustic soda. This operation [11] was twice repeated, the ether extract was dried with potash and the ether was distilled. The yield was 5.3 g (34%); the b.p. was 248-254°; the m.p. of the picrate was 179°; the m.p. of the methyl iodide derivative was 220°.

2. 7-Methylquinaldine. To 2.5 g of sodium, 100 ml of isobutyl alcohol and 14.9 g of m-acetotoluidide were added 15 ml of paraldehyde and the mixture was boiled with stirring for 3.5 hours. The subsequent treatment of the mixture was the same as that described in experiment 1. After the ether had been distilled the mixture of 5- and 7-methylquinaldines gradually solidified. The yield was 5.2 g (33%); the b.p. was 260-262°; the m.p. was 58-59°. When treated with alcoholic picric acid, a mixture of the picrates of 5- and 7-methylquinaldines with an m.p. of 182-185° was formed, indicating a considerable predominance of the picrate of 7-methylquinaldine. (According to Spivey and Curd [10]: a mixture of 5- and 7-methylquinaldines obtained by the Doebner-Miller reaction consists of 18% 5-methylquinaldine and 82% 7-methylquinaldine. The picrate of 7-methylquinaldine melts at 196°, and that of 5-methylquinaldine at 222°). After the bases had been washed with a small amount of isopropyl alcohol and filtered on a glass filter [10], transparent needles of 7-methylquinaldine (5-methylquinaldine-liquid) with an m.p. of 60-61° remained; the m.p. of the picrate was 193-194°.

3. 8-Ethoxyquinaldine. 2.3 g of sodium was dissolved in 80 ml of isobutyl alcohol and 17.9 g of o-acetophenetidide (m.p. 79-80°) was added with stirring; 14 ml of paraldehyde was then introduced rapidly. The mixture was boiled moderately for 3.5 hours, and a further 2-3 hours after the addition of 40 ml of water and 40 ml of concentrated hydrochloric acid. The alcohol was steam distilled and the 8-ethoxyquinaldine was precipitated as the salt with ferrocyanic acid by the addition of potassium ferrocyanide. The precipitate was filtered and decomposed with 10% caustic soda. The yield was 6.1 g (33%); the m.p. was 48-49°.

4. 7,8-Benzoquinaldine. 2.3 g of sodium, 80 ml of isobutyl alcohol, 18.5 g of acenaphthalide and 13.5 ml of paraldehyde were taken. The reaction was carried out in a similar way to experiment 1. After the alcohol had been distilled, 7,8-benzoquinaldine was precipitated as the salt with ferrocyanic acid, and after decomposition of the salt the impurities were removed with phthalic anhydride, as in experiment 1. The yield was 4.8 g (25%); the b.p. was 308-330°; the m.p. of the picrate was 225°.

5. 6-Chloroquinaldine. 3 g of sodium, 100 ml of isobutyl alcohol, 17 g of p-chloroacetanilide and 15 ml of paraldehyde were taken. The reaction was carried out in a similar way to experiment 1. After the alcohol had been distilled the residue was made alkaline and was steam distilled. Lustrous transparent plates formed in the condenser. The yield was 4.6 g (26%); the m.p. was 93°; the m.p. of the picrate was 204°.

6. 8-Chloroquinaldine. 3 g of sodium, 100 ml of isobutyl alcohol, 17 g of o-chloroacetanilide and 15 ml of paraldehyde were taken. The experiment was carried out and the quinaldine base was precipitated in the same way as described in experiment 5. The yield was 3.5 g (20%); the m.p. was 68°; the m.p. of the picrate was 173-174°.

7. Quinaldine. 12.1 g of formanilide was dissolved in 50 ml of alcohol, and a solution of 4.1 g of caustic soda in 10 ml of water was added gradually with stirring; 13.5 ml of paraldehyde was then added and the mixture was heated to boiling for 3.5 hours. The subsequent operations were similar to those described previously [1]. The yield was 5.4 g (38%); the b.p. was 238-248°, the m.p. of the picrate was 191°, the m.p. of the methyl iodide derivative was 194-195°.

8. 6-Methylquinaldine was obtained in a similar way to that described in experiment 7. The yield was 45%; the b.p. was 115-121° (2 mm); the m.p. was 59°; the m.p. of the picrate was 187-188°; the m.p. of the methyl iodide derivative was 241°.

9. 6-Methoxyquinaldine. 15.1 of formo-p-anisidide was dissolved in 60 ml of isobutyl alcohol; 4.1 g of caustic soda in 10 ml of water was added, and then 13.5 ml of paraldehyde. The reaction was carried out and the quinaldine base was precipitated in the same way as described in [1]. The yield was 5.1 g (30%); the m.p. was 280-292°; the m.p. was 63-64°; the m.p. of the picrate was 216-217°; the m.p. of the methyl iodide derivative was 236°.

SUMMARY

A number of quinaldine bases were synthesized by a previously developed modification of the Doebner-Miller reaction and the mechanism of the individual stages of the synthesis was examined.

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THE INVESTIGATION OF TAUTOMERISM IN NONPOLAR MEDIA

TAUTOMERIC EQUILIBRIUM OF THIOACIDS OF PHOSPHORUS IN BENZENE AND CHLOROBENZENE

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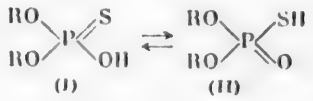
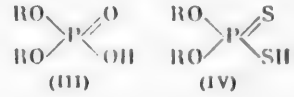
Several years ago we investigated the tautomeric equilibrium of dialkyl thiophosphoric acids (I ⇌ II) [1]



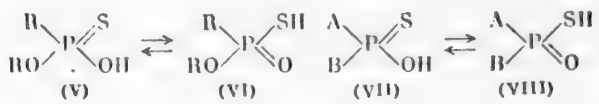
(I) (II)

in aqueous-alcoholic media by a potentiometric method based on the application of the Bronsted-Izmailov law to ionization constants of tautomeric acids [2]. The method is associated with the use of reference nontautomeric substances belonging to the same chemical type as the investigated tautomeric forms. Dialkyl phosphoric acids (III), of both the OH-acid and dialkyl dithiophosphoric acid (IV) type and the SH-acid type were used as the reference substances.



(III) (IV)

The ionization constants of both these types of acids and tautomeric dialkyl thiophosphoric acids in 7 and 80% alcohol were determined.* It was found that in 7% alcohol the tautomeric equilibrium of dialkyl thiophosphoric acids is displaced towards the thiolic forms (II), and in a medium of 80% alcohol, towards the thionic forms (I). When the tautomerism of acid esters of alkyl thiophosphinic acids was investigated by this method [4] it was established that the tautomeric equilibrium is displaced almost entirely towards the thionic forms (V) in both 7% and 80% alcohol. The influence of structure on the tautomeric equilibrium of thioacids of phosphorus with the general formula



(V) (VI) (VII) (VIII)

* These data were subsequently improved [3].

with a wide range of variation of the A and B radicals was later [3] investigated in detail. The investigation was based on the use of Hammett's equation for the ionization constants of tautomeric acids, the tautomeric equilibrium constants being calculated from deviations from Hammett's linear law. It was found that the principal factors determining the position of the thion-thiolic equilibrium of thioacids of phosphorus are the polarity of the medium and the nature of the radicals combined with the phosphorus. An increase in the polarity of the medium (changeover from 80% alcohol to 7%) and the use of radicals with high σ values (i.e., electron acceptor) displaces the equilibrium towards the thiolic forms.

There was justification for the assumption that in nonpolar media with a low dielectric constant the tautomeric equilibrium of thioacids of phosphorus will be displaced towards the thionic forms for any phosphorus-containing radicals. The aim of the present investigation was to check this assumption.

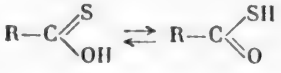
In contrast to conducting protolytic media in which the prototropic tautomeric equilibrium consists of the equilibrium of the tautomeric forms of acids or bases with the corresponding ions, in nonpolar media with a low dielectric constant ionic pairs are in equilibrium with the molecular tautomeric forms. In the case of the tautomerism of substances of acid character the ionic pair is formed by an anion and cation of the base-proton carrier, common to both tautomeric forms. In weakly polar media dissociation of ionic pairs to free ions is very slight and has no effect on the position of tautomeric equilibrium. From all the data, the general system of tautomeric equilibrium in nonpolar media with a low dielectric constant can be represented as follows [5].

$$\begin{array}{c} A_1H + B \rightleftarrows A_1H \ldots B \rightleftarrows [A^-HB^+] \rightleftarrows A_2H \ldots B \rightleftarrows A_2H + B \\ \downarrow\uparrow \\ A^- + HB^+ \end{array} \quad (1) \qquad (1)$$

Outside the dependence on the possible dissociation of ionic pairs the tautomeric equilibrium constant in nonpolar media must be equal to the ratio of the constants of the protolysis of tautomeric forms by the base-proton carrier

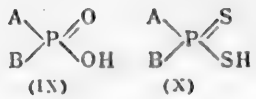
$$K_T = \frac{K_{A_1B}}{K_{A_2B}}. \qquad (2)$$

Two of the authors recently [6] developed an optical method for determining the protolysis constants of acids in nonpolar media by the use of an indicator-base, employed in stoichiometric amounts with respect to the acid and consequently playing a double role: a base, producing the specific buffering of the solution, and an indicator. It was found that in benzene and chlorobenzene, the protolysis constants of carboxylic acids with crystal violet base obey Bronsted's law satisfactorily: a linear relation is observed between the logarithms of the protolysis constants in benzene and chlorobenzene, the angle of inclination of the straight line being close to 45°. The protolysis constants of dithiocarboxylic acids RCSSH were then investigated; these also obeyed Bronsted's law. As was expected, within the coordinates pK_{AC_1} and pK_{AS_2} ($S_1 = C_6H_6$; $S_2 = C_6H_5Cl$) the dithioacids formed their own straight line parallel to the straight line of the carboxylic acids. It was, therefore, possible to investigate the tautomerism of monothiocarboxylic acids [5] on the same basis as that for the investigation of the tautomerism of monothiophosphoric acids, the only difference being that the protolysis constants must be used instead of the ionization constants. It was found that in benzene and chlorobenzene the tautomeric equilibrium is displaced towards the thiolic forms.



This conclusion was confirmed by an independent spectral investigation and it was thus proven that the protolysis constants can be used for determining the position of tautomeric equilibrium.

In the present work we investigated the protolysis of oxy and thioacids of phosphorus with hexamethoxy red indicator in benzene and chlorobenzene. Oxy acids of phosphorus, of the general type (IX), were used as the reference OH acids; dithioacids of phosphorus, of type (X), were used as reference SH acids; acids (VII ⇌ VIII) with interchange of the A and B radicals were used as the tautomeric acids.



(IX) (X)

The optical densities of the solutions of acid and indicator, taken in equivalent or simple multiple ratios of the concentrations a_0 and b_0, were determined by means of an electrophotocolorimeter; the concentration of the colored form of the indicator (f) was determined by the ordinary calibrated curve method (standard – a specific amount of indicator with a 100-fold excess of a benzene solution of hydrogen chloride) and the protolysis constants (K_{AB}) and the indices of the power n on characterizing the number of particles formed by a protolytic reaction [6] were then calculated by means of equation (3). The measurements were carried out at room temperature without thermostatic control. The values are $a_0 \cong 10^{-3}$, $b_0 \cong 10^{-4}$.

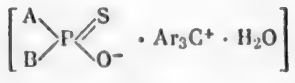
$$K_{AB} = \frac{f^n}{(a_0 - f)(b_0 - f)} \qquad (3)$$

The results obtained are given in the Table.

Protolysis Constants of Phosphorus Acids with Hexamethoxy Red in Benzene and Chlorobenzene

Numbering of points on the graphs	Formula	n		pK_{AB}	
		in benzene	in chlorobenzene	in benzene	in chlorobenzene
1	$(C_2H_5O)_2PSOH$	1.05	1.06	—1.69	—2.13
2	$(C_3H_7O)_2PSOH$	1.07	1.06	—1.52	—1.84
3	$(Iso\text{-}C_4H_9O)_2PSOH$	1.04	1.07	—1.46	—1.87
4	$CH_3(C_2H_5O)PSOH$	0.99	1.03	—1.01	—1.28
5	$CH_3(C_3H_7O)PSOH$	1.01	1.06	—0.87	—1.12
6	$CH_3(C_4H_9O)PSOH$	1.00	1.06	—0.67	—1.12
7	$Iso\ C_4H_9(C_4H_9O)PSOH$	1.10	1.10	—0.39	—0.73
8	$(C_2H_5O)_2PSSH$	0.99	1.01	—0.89	—1.73
9	$(C_4H_9O)_2PSSH$	1.00	1.01	—0.62	—1.45
10	$(Iso\ C_4H_9O)_2PSSH$	1.00	1.00	—0.74	—1.66
11	$CH_3(C_3H_7O)PSSH$	0.94	0.97	—0.13	—0.94
12	$(C_2H_5O)_2POOH$	1.01	1.08	—0.17	—0.43
13	$(C_6H_5O)_2POOH$	1.01	1.05	—2.09	—2.57
14	$(p\text{-}CH_3C_6H_4O)_2POOH$	1.10	1.10	—1.40	—1.65
15	$ClCH_2(p\text{-}CH_3C_6H_4O)POOH$	1.07	1.06	—1.66	—2.20

Since the indices of the power n are equal, within the limits of experimental error, to 1, the protolysis of phosphorus acids with the indicator hexamethoxy red leads to the formation of one molecule, a hydrated ionic pair of the type:



If a graph is plotted within the coordinates pK_{AB} benzene and pK_{AB} chlorobenzene on the basis of the data obtained, it is seen (Fig. 1) that oxy and dithioacids of phosphorus form two parallel straight lines with an angle of inclination close to 45°. Monothioacids (1-7) are characterized by points lying, within the limits of experimental error, on the straight line of oxyacids, i.e., OH acids. The conclusion follows, therefore, that the tautomeric equilibrium of monothioacids of phosphorus in benzene and chlorobenzene is displaced almost completely towards the thionic forms.

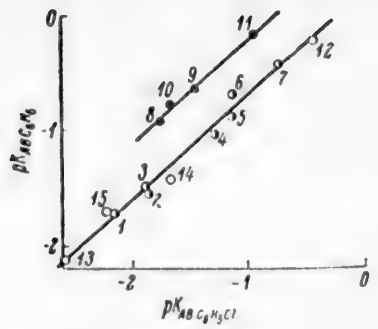


Fig. 1. Relationship between the indices of the protolysis constants (pK_{AB}) of phosphorus acids with hexamethoxy red in benzene and chlorobenzene.*

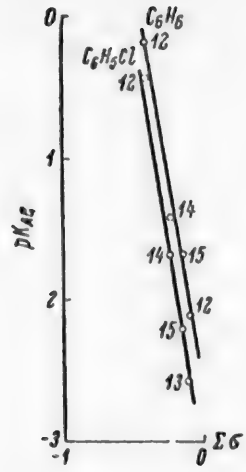


Fig. 2. Relationship between pK_{AB} and $\Sigma\sigma$ for dialkyl and diaryl phosphoric acids (from our data the value of σ for $ClCH_2$ was calculated as 0.050).

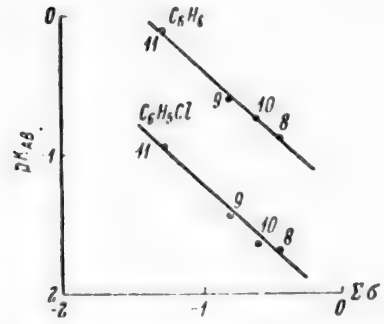


Fig. 3. Relationship between pK_{AB} and $\Sigma\sigma$ for dithiophosphoric acids.

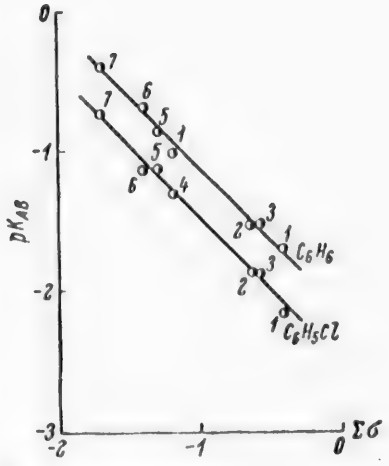


Fig. 4. Relationship between pK_{AB} and $\Sigma\sigma$ for monothiophosphoric acids.

The same conclusion can be reached from an examination of the influence of radicals combined with phosphorus on the protolysis constants of acids. In Figs. 2-4 the results obtained are given within the coordinates pK_{AB} and $\Sigma\sigma$ [7]. As may be seen, a satisfactory linear Hammett relation, without deviations, is observed. It was previously shown [3] that the strict observance of the linear Hammett relation for the ionization constants of tautomeric substances indicates the displacement of the tautomeric equilibrium towards one of the forms. There is justification for the assumption that this is equally true for the protolysis constants of tautomeric acids with an indicator-base. Here (Fig. 4) too, therefore, we reach the conclusion that tautomeric equilibrium is displaced toward one of the forms. In the given case the fact that this form is thionic follows from a comparison of the results obtained during an investigation of aqueous, alcoholic, benzene and chlorobenzene solutions. As one passes from water to alcohol the equilibrium is displaced from the thiolic forms to thionic. Hence, in media which are still polar it is displaced all the more towards the thionic forms.

* Here, and in the other diagrams, see Table for the numbering of the points.

Hence, both methods, based on quite different assumptions, lead to the conclusion that, in contrast to thiocarboxylic acids, the tautomeric equilibrium of thioacids of phosphorus in benzene and chlorobenzene is almost completely displaced towards the thionic forms. The cause of the difference in the behavior of thiocarboxylic and thiophosphoric acids must be discussed.

It may be thought that the difference in the behavior of these types of acids is due to the differences in the basicity of P = O and P = S groups on the one hand and C = O and C = S groups on the other. It is known that the P = O group has more markedly expressed basic properties than the C = O group. The basic properties of P = S and C = S groups are weaker than the P = O group. In the HS-P = O combination of atoms the proton passes readily from sulfur to oxygen, which is the most basic point of a molecule forming a stable combination S = P-OH. Since electron-acceptor substituents reduce the basic properties of the P = O group they have little influence on the acidic properties of the SH group; these substituents therefore assist the appearance of the thiolic form. As a result of their leveling effect on the strength of acids and the possibility of the formation of hydrogen bonds with P = O and HS groups (but not with a P = S group), polar hydroxyl-containing solvents also assist the thiolic form.

The basic properties of the C = O group of thiocarboxylic acids are inadequate for stable combination of a proton in the form S = C-OH. This is particularly clearly indicated in the presence of electron-acceptor substituents (in all media, p-nitrobenzoic acid has a thiolic structure). In the presence of electron-donor substituents the basic properties of the C = O group are increased, and in equilibrium the thionic form appears. This is more clearly shown in polar solvents with a leveling effect. Thus, electron-donor radicals and thiocarboxylic acids and thiophosphoric acids assist the thionic form, while electron-acceptor radicals assist the thiolic form. But in the former the thiolic form is more stable, while in the latter it is the thiolic form which is the most stable; in the case of the former, polar solvents therefore assist an increase in the concentration of the thionic forms, whereas in the latter they increase the concentration of the thiolic forms.

The methods of obtaining all the measured acids and their constants have been previously described.

SUMMARY

1. The protolysis constants of a number of oxy, dithio and monothiophosphoric acids with hexamethoxy red indicator in benzene and chlorobenzene were measured by the colorimetric method.

2. By a method based on the Bronsted-Izmailov theory and a comparison of the indices of the protolysis constants with $\Sigma\sigma$ it was established that the tautomeric equilibrium of thioacids of phosphorus in benzene and chlorobenzene is displaced almost completely towards the thionic forms.

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• Original Russian pagination. See C. B. Translation.

THE SUBSTITUTION OF HALOGEN IN NITROGEN COMPOUNDS

XII. THE INFLUENCE OF THE NATURE OF THE HALOGEN

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It is of interest to obtain comparative data on the substitution of different halogens in o-halogen-o'-oxyazo compounds, both for determining more accurately the boundaries of the applicability of a given reaction and establishing its mechanism.

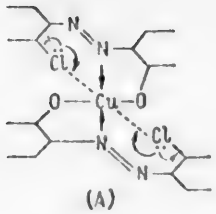
The investigation of the reaction kinetics of the substitution of halogen in azo compounds involves considerable difficulties due to the selection of a medium in which the reaction is homogeneous over its whole duration and conditions in which it takes place at a velocity suitable for measurement. Numerous preliminary experiments showed that in the case of 2-halogenbenzene-(1-azo-1')-naphthols-2' satisfactorily reproducible results are obtained by reacting with sodium methylate in the presence of copper acetate in a mixture of methanol and dioxane, in which both the initial substances and the reaction products are soluble, provided that the original concentrations of the initial substances are fairly low (about 10^{-3} g-mole/liter for the nitro compound).

Control of the reaction was effected by determining the amount of free halogen in the wash water. To determine the nature of the reaction products formed during the reaction with the sodium methylate, exhaustive halogen substitution experiments were carried out; the reaction products were isolated, purified and identified. In all cases in which a substitution reaction of halogen under the conditions investigated takes place, 2-methoxybenzene-(1-azo-1')-naphthol-2' was isolated as the reaction product; it was identified by a mixed melting point with the compound obtained by synthesis from o-anisidine and 2-naphthol [1].

The experiments showed that at 100°, i.e., under conditions where the chlorine atom in 2-chlorobenzene-(1-azo-1')-naphthol-2' is quantitatively replaced by an alkoxy group in 2 hours [2], the fluorine atom in the analogous compound is not completely replaced in even 8 hours. As regards bromine and iodine, these halogens are quantitatively replaced by reaction with sodium methylate in 1 hour at 30° and under conditions in which the chlorine atom is only 8% replaced. To determine the difference in the mobility of bromine and iodine in azo compounds, experiments were carried out at lower temperatures; these indicated that the iodine atom is replaced somewhat more readily than the bromine atom (82 and 62% respectively in 30 minutes at 20° and 65 and 60% in 30 minutes at 10°).

Thus, with respect to ease of replacement by alkoxy groups in analogous o-halogen-o'-oxyazo compounds in the presence of a copper salt, halogens behave in the order: $F \ll Cl < Br < I$. This series is the reverse from that for the reaction of sodium alcoholates with 4-nitro and 2,4-dinitrohalogenbenzenes [3].

It is noteworthy that in the above-mentioned series the increase in the mobility of the halogen atom in an azo compound is parallel to the reduction in their electronegativity [4] and the increase in the polarizability of the C-Hal bond [5]. This is explained if we assume [6] that the cause of the increased mobility of the halogen atoms in o- and peri-halogen-o'-oxyazo compounds in the presence of a copper salt is their reaction with a metal atom in the intermediate complex (A),



(A)

leading to a weakening of the C-Hal bond and assisting the splitting off of halogen in the form of an anion.* The high electronegativity of the halogen will evidently impede the formation of its bond with the copper atom in the complex. At the same time, the high polarizability of the C-Hal bond will assist the displacement of the electron shell towards the central atom of copper, thus paralyzing the effect of the conjugation of unshared halogen electrons with the π-electrons of the aromatic nucleus, imparting increased strength to the C-Hal bond in aromatic halogen derivatives.

EXPERIMENTAL

2-Chlorobenzene-(1-azo-1')-naphthol-2' (I), m.p. 167° (mean [7]).

2-Bromobenzene-(1-azo-1')-naphthol-2' (II), m.p. 174.5-175° (from a mixture of ethanol and chlorobenzene, 3:1); according to [8]: m.p. 165° (from benzene).

2-Iodobenzene-(1-azo-1')-naphthol-2' (III), m.p. 178-178.5° (from a mixture of methanol and chlorobenzene, 3:1); according to [9]: m.p. 176°.

Preparation of 2-fluorobenzene-(1-azo-1')-naphthol-2' (IV). A solution of 0.6 g of sodium nitrite in 5 ml of water was added to a solution of 1 g of o-fluoroaniline (b.p. 58-60° at 11 mm, mean [10]) in 3 ml of concentrated hydrochloric acid in 5 ml of water, cooled to 0° by the addition of 10 g of ice. The diazo solution obtained was added for 1 hour to a suspension of the 2-naphtholate obtained from 1.14 g of 2-naphthol, 1.6 ml of a 30% solution of caustic soda, 2.1 g of soda and 12 ml of water. The dark-red precipitate was filtered, washed with water and dried. The weight was 2.2 g (92%); recrystallization from ethanol gave fine dark-red needles with an m.p. of 124.5-125.8°. It was soluble in benzene, toluene, methanol, ethanol and dioxane.

Found %: C 72.61, 72.46; H 4.34, 4.48; N 10.33, 10.43. $C_{16}H_{11}ON_2F$. Calculated %: C 72.19; H 4.14; N 10.52.

Reaction of azo dyes with sodium methylate. A mixture of solutions of 0.0625 g of copper acetate in 30 ml of methanol and $6.25 \cdot 10^{-4}$ g-mole of dye in 50 ml of dioxane was added to a solution of sodium methylate obtained by the reaction of 0.72 g of sodium with 20 ml of methanol. The mass while being stirred was kept at the predetermined temperature, for a specific time 20 ml of 10% sulfuric acid and 100 ml of benzene were added and the solution of dye was thoroughly washed with distilled water. The aqueous layer and the wash water were added to a 250 ml measuring flask and the halogen content was determined in 10 ml samples by potentiometric titration with a 0.005 N solution of silver nitrate (P-4 potentiometer, with silver and calomel electrodes). The amount of halogen split off was calculated with respect to the amount contained in the initial halogenazo compound. The presence of fluorine in the wash water was checked by the reaction with zirconium oxychloride in the presence of sodium alizarin sulfonate [11]. The results of the experiments are given in the Table.

Precipitation of 2-methoxybenzene-(1-azo-1')-naphthol-2'. In the experiments with dyes (I), (II), and (III), after the reaction had been carried out for a period sufficient for exhaustive substitution of the halogen atom (which was checked by potentiometric titration of the wash water of the reaction mass after acidification) the solvents were distilled under vacuum. The residue was boiled with 20% hydrochloric acid, after which the dye was purified by recrystallization from glacial acetic acid and identified by a mixed melt with the azo dye from o-anisidine and 2-naphthol (m.p. 178° [1]).

* In the paper by N. N. Vorozhtsov, G. G. Yakobson and T. D. Rubina, published in September 1959 (Doklady Akad. Nauk SSSR 127, 1225), a similar series of halogen activity was given for the catalytic ammonolysis of halogen derivatives of benzene, and a completely similar explanation was given.

Initial dye	Reaction temp.	Duration of reaction (min)	0.005 ml $AgNO_3$ used in the titration (ml)	Amount of halogen in the reaction mass (%)
(I)	30°	60	0.39, 0.43 Mean 0.41)	8.2
(II)	30	60	20.10, 19.80 " 19.95) •	100.2
(III)	30	60	4.92, 4.94 " 4.93)	98.6
(II)	20	30	3.09, 3.11 " 3.10)	62.0
(II)	20	30	3.09, 3.09 " 3.09)	61.8
(III)	20	30	4.06, 4.04 " 4.05)	81.0
(III)	20	30	4.15, 4.17 " 4.16)	83.2
(II)	10	60	3.03, 3.01 " 3.02)	60.4
(III)	10	60	3.23, 3.27 " 3.25)	65.0
(IV)	100	480 ••		

• Back titration: amount of wash water (ml) required in the titration of 10 ml of 0.01 N $AgNO_3$.

•• On completion of the reaction the initial product was quantitatively precipitated [T. D. Rubina and N. I. Krizhechkovskaya took part in the experiments with dye (IV)].

SUMMARY

1. The reaction of 2-fluoro, 2-chloro, 2-bromo and 2-iodobenzene-(1-azo-1')-naphthol-2' with sodium methylate in the presence of copper acetate was investigated. It was established that the halogen atoms are arranged according to ease of substitution in the given reaction in the following order: F ≪ Cl < Br < I, the fluorine atom being hardly replaced by an alkoxy group when heated for 8 hours at 100°, whereas bromine and iodine atoms are replaced quantitatively in 1 hour at 30°.

2. Proposals are put forward to substantiate the relationship between the degree of mobility of the halogen atoms in azo compounds and their electronegativity and the polarizability of the C-Hal bond.

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THE NUMBER OF RADICALS THAT MAY BE LINKED DIRECTLY WITH A METAL ATOM

I. ORGANOTIN COMPOUNDS

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Numerous investigations in the field of organometallic compounds have shown that the number of radicals bound directly to the metal atom does not always correspond with its valence. By using organomagnesium reactions it has not been possible, for example, to combine four tertiary butyl, or four tertiary amyl radicals with an atom of tin. Only compounds of the type R_3SnCl are obtained [1]. It has only been possible to combine two tertiary butyl radicals with silicon by using lithium [2]. On the other hand, the number of tertiary butyl radicals that may be combined with an atom of boron corresponds with its valence, namely, three [3]. Many similar examples are described in the literature.

The number of radicals present in a given organometallic compound undoubtedly depends on the degree of branching of the alkyl radicals or on the presence and character of the ortho substituents in aryl radicals, as well as on the strength of the bonds joining the radicals to the metal atom.

For any given radicals, however, there must exist a numerical limit which cannot be exceeded even by the use of the most active reagents. The determination of this limit and other laws for the combination of radicals directly with a metal atom has great theoretical and practical significance.

The explanation of the possible number of mesityl and other diortho-substituted aryl radicals, containing such simple groups as CH_3, CH_3O, C_2H_5O as ortho substituents, that can be joined directly to an atom of tin is the purpose of the present study.

The interaction of mesityl magnesium bromide with tin tetrabromide, in the presence of an excess of the first reagent, leads to the formation of trimesityl tin bromide. Neither raising the temperature of the reaction mixture (to 154°), nor prolonging the time of heating (to 20 hours), nor increasing the quantity of the Grignard reagent (up to 20 moles per mole of $SnBr_4$), changed the results of the experiment. Trimesityl tin bromide remained as the final product of the reaction. Treating trimesityl tin bromide with an excess quantity of more active reagents such as mesityl lithium, mesityl sodium or mesityl potassium failed to give tetramesityl tin.* This indicates the practical impossibility of joining four mesityl radicals to an atom of tin.

With the aim of ascertaining the agreement of this conclusion with the theoretical possibility of placing four mesityl radicals about an atom of tin, calculations were made on the magnitude of the intersection of the ortho substituents (the carbon atoms of the methyl groups) of the mesityl groups in their various locations in space.

* The work of Bahr and Gelius [4], who supposedly obtained tetramesityl tin (m.p. 320°) by the interaction of mesityl lithium with $SnCl_4$ in boiling toluene, has been shown to be erroneous. We repeated their experiments several times under identical conditions, but only succeeded in separating trimesityl tin chloride and dimesityl tin oxide (m.p. above 200°), but tetramesityl tin did not appear among the reaction products.

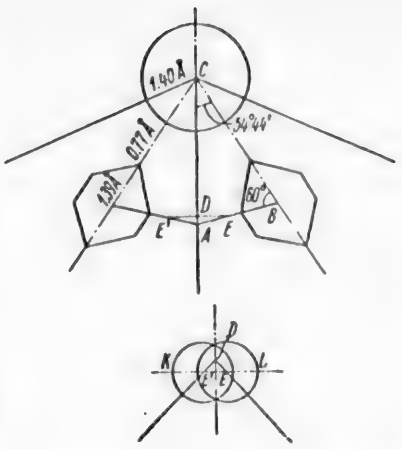

Fig. 1.

The maximum degree of intersection of two atoms of carbon, which are part of the methyl groups and located in the ortho position, will occur when three mesityl radicals (out of four) are located on the planes of a triangular pyramid, the edges of which form a tetrahedral angle (109°28').

If we take the covalent radii of the atoms of tin and carbon of the aromatic ring, and the ordinary bond distance between the methyl carbon and the aromatic group as equal to 1.40, 0.77, 1.39 and 1.54 Å, then the magnitude BC = 3.56 Å (Fig. 1), while AB = BC sin 54°44'/ / sin 65°16' = 3.20 Å. Consequently the center of the carbon atom of the ortho substituent (the methyl group) is located on the straight line AB, at a distance from the edge equal to 3.20 − (1.39 + 1.54) = 0.27 Å. The perpendicular line ED from the center of the carbon atom to a line passing along the edge of the pyramid is equal to ED = AE · sin 65°16' = = 0.27 Å. sin 65°16' = 0.245 Å. Two lines perpendicular to the edge, and located in different planes of the pyramid, form an angle between them which is equal to 120°. This makes possible the calculation of the distance between the centers of two atoms of carbon of the methyl groups in neighboring mesityl radicals, and, consequently, the degree of intersection of the carbon atoms of the ortho substituents.•

$EE'/2 = DE \cdot \sin 60° = 0.245$ Å $\cdot \sin 60° = 0.212$ Å; $EE' = 0.42$ Å.

Consequently, KL = 1.54 + 0.42 = 1.96 Å. Designating the magnitude of intersection by J, we find J = 2 (1.54)− − 1.96 = 1.12 Å.

As the angle formed by the edges of the pyramid increases, the degree of intersection of two carbon atoms of the methyl groups will naturally decrease and will become minimal (0.44 Å) if three mesityl radicals are located in one plane (the angle formed by the valences is equal to 120°). With such a maximum (1.12 Å) or minimum (0.44 Å) intersection of the carbon atoms in ortho positions, is a similar distribution of the mesityl radicals joined to the tin atom possible? From the work of Adams [5, 6] concerning the optical isomers of biphenyl compounds, it follows that groups located in the meta position have a repelling effect on ortho substituents and defect them, thus strengthening the intersection of the latter, in consequence of which the free rotation of the phenyl rings is impossible and optical activity appears. These studies indicate the possibility of some deflection of the ortho substituents from their natural disposition in space. Knowing this, it is possible to assume, as the first of the possible variants, a distribution of the mesityl radicals in trimethyl tin halides with the mesityl radicals located in one plane (the angle formed by the valences is 120°; the deflection of the ortho-methyl groups is 0.22 Å) or in positions near to this.

A second possible variant is that the mesityl radicals are rotated on some corner. If the first mesityl radical is located in the plane of a trihedral pyramid (the angle between the edges being equal to 109°28'), and the second mesityl radical is located perpendicular to the plane of the pyramid, then, since the effective thickness of the aromatic ring is 3.70 Å [7] and the covalent radius of a hydrogen atom is 0.30 Å, the magnitude of intersection (J) when a hydrogen atom of the methyl group is in one plane with the benzene ring will be equal to 0.38 Å. When the hydrogen atom is deflected from the former position by a 54°44' angle, the atoms of hydrogen will be located at a distance of 0.18 Å from the second mesityl radical; i.e., there will be no intersection. Neither will there be any intersection in the arrangement of three mesityl radicals joined to a tin atom, if the planes of the benzene rings of the mesityl radicals are located under an angle of 45° to the planes of the pyramid (the angle between the edges is 109°28'). This same conclusion can be drawn in relation to the arrangement of four mesityl radicals in tetramesityl tin. The arrangement under a 45° angle will be the most satisfactory arrangement of mesityl radicals in which no intersection of groups will be observed.

Since the above geometric data suggest the possibility of placing four mesityl radicals about an atom of tin and while, on the contrary, the results of experiments indicated the practical impossibility of combining a fourth mesityl radical to an atom of tin, the solution of the problem of the most probable spatial distribution of three mesityl radicals in trimesityl tin bromide which makes it impossible to replace a halogen by a fourth mesityl radical may be found by studying the nature of a fourth radical which is able to combine with an atom of tin in the presence of three mesityl groups.

• The hydrogen atoms of the methyl groups are not taken into consideration.

Replacement of an Atom of Bromine by a Fourth Radical in Trimesityl Tin Bromide

Compound added to trimesityl tin bromide	Bromine content (%) in the reaction product depending on the ratio of the second component to trimesityl tin bromide				Name of the reaction product $[C_6H_2(CH_3)_3]_3SnR$•	M.p.	Solvent for recrystallization	Empirical formula	% Sn	
	5 times	8 times	10 times	20 times					found	calculated
Methyl magnesium iodide••	0.0	–	–	–	Methyltrimesityl tin	155°	Petroleum ether	$C_{28}H_{36}Sn$	24.01	24.16
Ethyl magnesium bromide•••	6.4	3.5	2.0	0.0	Ethyltrimesityl tin	143.5	Petroleum ether	$C_{29}H_{38}Sn$	23.25	23.49
n-Propyl magnesium bromide	7.3	4.2	2.8	Traces	n-Propyltrimesityl tin	130	Alcohol	$C_{30}H_{40}Sn$	22.82	22.84
n-Butyl magnesium bromide	7.0	3.8	2.2	0.0	n-Butyltrimesityl tin	118.5	Alcohol	$C_{31}H_{42}Sn$	22.19	22.24
n-Hexyl magnesium bromide	–	–	7.5	3.0	n-Hexyltrimesityl tin	115	Alcohol	$C_{33}H_{46}Sn$	21.01	21.14
n-Octyl magnesium bromide	–	–	2.5	Traces	n-Octyltrimesityl tin	104.5	Alcohol	$C_{35}H_{50}Sn$	19.83	19.80
Isopropyl magnesium bromide	8.2	5.1	3.5	1.1	Isopropyltrimesityl tin	146.5	Petroleum ether	$C_{30}H_{40}Sn$	22.66	22.84
Isobutyl magnesium bromide	–	–	3.7	1.2	Isobutyltrimesityl tin	100	Alcohol	$C_{31}H_{42}Sn$	22.00	22.24
Isoamyl magnesium bromide	–	–	3.7	1.0	Isoamyltrimesityl tin	107	Alcohol	$C_{32}H_{44}Sn$	21.70	21.68
Phenyl magnesium bromide	11.5	–	8.0	3.5	Phenyltrimesityl tin	143	Petroleum ether	$C_{33}H_{38}Sn$	21.48	21.45

•All compounds are described for the first time.

••Reaction conditions: 42°, heated for 3 hours, solvent: ether-benzene mixture.

•••Reaction conditions: 115°, heated for 12 hours, solvent: toluene. In all subsequent experiments the same conditions were maintained.

As has been shown in a number of experiments, the results of which are given in the table, it is comparatively easy to replace the bromine in trimesityl tin bromide by primary alkyl radicals even with comparatively long hydrocarbon chains; its replacement by secondary radicals is more difficult. It cannot be replaced by tertiary radicals. It is possible to join a phenyl radical as a fourth radical to an atom of tin linked to three mesityl radicals, but it is not possible to join an o-tolyl grouping to an atom of tin even by treatment of trimesityl tin bromide by an excess of o-tolyl lithium. Halogen atoms (chlorine, bromine, iodine) easily unite with an atom of tin which is linked with three mesityl radicals.

By comparing the results of the geometrical calculations and the experimental facts, it is possible to draw the following conclusion concerning the most probable arrangement of three mesityl radicals in the compounds enumerated above: three mesityl radicals are arranged in the planes of a three-sided pyramid, the edges of which form an angle approaching 120°. The atom of tin is located at the vertex of this pyramid. Undoubtedly the tendency of the tin electrons to couple with the π-electrons of the aromatic rings will favor a similar spatial arrangement of groups.

Similar arrangement of atoms at the corners of very flat pyramids are well-known in chemistry. For example, the distance between the atoms of chlorine in chloroform, as determined by x-ray interferometer studies, has permitted the determination of the fact that the angle between the atoms of chlorine and carbon is equal to 116°, while in methylene chloride it is 124° [8]. Only by the arrangement of the mesityl radicals as pointed out above is it possible to explain the impossibility of replacing bromine in trimesityl tin bromide by ortho-tolyl and also by mesityl radicals. With an effective thickness of the aromatic ring of 3.70 Å, a carbon atom of the methyl group, combined with the radicals mentioned, must undergo considerable deflection, the maximum magnitude of which is equal to 0.53 Å (Fig. 2), which is scarcely possible.

$$DO = DE + EF + FO = 1.39 + 0.77 + 0.77 = 2.93 \text{ Å}$$
$$DL = DO \cdot \sin 30° = 2.93 \cdot \sin 30° = 1.47 \text{ Å}$$
$$DA = AB + BC + CD = 1.40 + 0.77 + 1.39 = 3.56 \text{ Å}$$
$$ML = 3.56 - (1.85 + 1.47) = 0.24 \text{ Å}$$

Consequently, the magnitude of intersection is J = 0.77 − 0.24 = 0.53 Å.

Organomagnesium compounds, obtained from 1-bromo-2-alkoxynaphthalenes, are stereochemically similar to diortho-substituted arylmagnesium halides, and therefore when they react with $SnBr_4$, they form compounds with tin that contain three radicals. Of a number of such compounds, tri-(2-methoxynaphthyl-1) tin bromide and tri-(2-ethoxynaphthyl-1) tin bromide were synthesized.

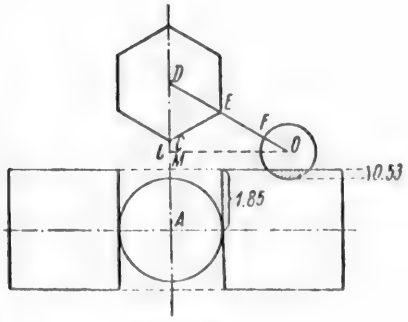

Fig. 2.

EXPERIMENTAL

Synthesis of trimesityl tin bromide. To an ether solution of mesitylmagnesium bromide, prepared from 50 g of bromomesitylene and magnesium, 27.4 g of tin bromide dissolved in ether was added drop by drop while the reaction mixture was cooled and stirred. The reaction mixture was heated on the water bath for six hours and was then decomposed by water and 10% hydrobromic acid. The ether layer was washed with water, then with a solution of sodium bicarbonate, again washed with water and then dried by means of sodium sulphate. After driving off the solvents the material remaining was crystallized. The crystals were purified by recrystallization from toluene. Melting point 178°. Yield 20 g (60%). Trimesityl tin bromide is soluble in benzene and toluene and is stable in the presence of water and air.

Found %: Sn 21.40; Br 14.40. $C_{27}H_{33}SnBr$. Calculated %: Sn 21.34; Br 14.37.

Increasing the quantity of tin bromide to 36.5 g led to the formation, along with trimesityl tin bromide, of a certain quantity of dimesityl tin dibromide. The latter hydrolyzes during the decomposition of the reaction mixture by the addition of hydrobromic acid, becoming dimesityl tin oxide, which separates out as a dense white precipitate that is insoluble in ordinary organic solvents. At 204-210° it begins to decompose.

Found %: Sn 32.03. $C_{18}H_{22}OSn$. Calculated %: Sn 31.82.

The replacement of tin bromide by 10 g of tin tetrachloride leads to the formation not of trimesityl tin chloride but of trimesityl tin bromide because of the substitution of the chlorine in the chloride first formed by bromine. Melting point 178°. A test by mixing with trimesityl tin bromide obtained in the first experiment showed no depression. A qualitative test for bromine (with fluorescein paper) was positive.

Synthesis of trimesityl tin iodide. To 3 g of trimesityl tin bromide dissolved in 30 ml of benzene were added 0.85 g of sodium iodide dissolved in acetone. After 30 minutes of boiling the cooled reaction mixture was filtered from the precipitated sodium bromide. The acetone-benzene solution was evaporated. The trimesityl tin iodide obtained, after recrystallization from toluene, showed a melting point of 212°.

Found %: 19.75; I 21.08. $C_{27}H_{33}SnI$. Calculated %: Sn 19.68; I 21.06.

Attempts to obtain tetramesityl tin. To a double quantity of mesityl lithium, prepared in the usual way in ether solution [9], was added an ether solution of trimesityl tin bromide (3 g). The reaction mixture was heated six hours. After the usual operations of decomposing the reaction mixture with water, washing, and drying the ether layer and then evaporating the solvent, unchanged trimesityl tin bromide separated out. Melting point 178°. A test by mixing with the starting material showed no depression. In subsequent experiments ether was replaced by benzene, toluene or xylene. The reaction mixture was heated for six hours. When benzene was substituted for ether, the reaction also failed. When toluene was used as a solvent and the quantity of mesityl lithium was increased from two to eight times in relation to the trimesityl tin bromide (1 g); from this substance by crystallization from toluene a colorless crystalline compound which did not contain bromine was obtained. Its melting point was 162° and its tin content was 24.90% (the tin content of trimesityl tin is 19.93%). The structure of this compound is being ascertained. The replacement of ether by xylene and boiling the reaction mixture for six hours led to the formation of a tarry product from which it was possible to separate only the starting product—trimesityl tin bromide (1.8 g, 60%).

Reactions of mesityl sodium and mesityl potassium (obtained in the usual way with a 40-50% yield) with trimesityl tin bromide, carried out successively in boiling petroleum ether (70-80° fraction), benzene, toluene, xylene and mesitylene (with heating for a 12 hour period), led to the formation of products consisting of the starting compound (65-30%) and a tarry substance from which it was impossible to separate crystalline compounds. In carrying out these reactions we of course took into account the possibility of the migration of the sodium or potassium into the side chain.

Synthesis of tri-(2-methoxynaphthyl-1) tin bromide. An ether solution of 2-methoxy-1-naphthyl magnesium bromide was prepared in the usual way from 15 g of α-brom-β-methoxynaphthalene, 2 g of magnesium and anhydrous ether (5 volumes). To the organomagnesium compound there was added, dropwise, a benzene solution (3 volumes) containing 6 g of tin bromide. After being heated for six hours the reaction mixture was decomposed by water and 10% hydrobromic acid. The ether-benzene solution was washed, dried over calcium chloride, and the solvent evaporated. Crystals were obtained from the remaining material (from toluene) with a melting point of 221°. The yield was 4 g (43%).

Found %: Sn 17.52; Br 11.76; OCH_3 13.7. $C_{33}H_{27}O_3SnBr$. Calculated %: Sn 17.71; Br 11.93; OCH_3 13.9.

Synthesis of tri-(2-ethoxynaphthyl-1) tin bromide. With the same relationship between reacting components, tri-(2-ethoxynaphthyl-1) tin bromide was prepared in an analogous manner. Melting point 217° (from toluene). Yield 38%.

Found %: Sn 16.48; Br 11.13; OC_2H_5 18.6. $C_{36}H_{33}O_3SnBr$. Calculated %: Sn 16.67; Br 11.22; OC_2H_5 19.0.

SUMMARY

1. Experimental proof is offered to show the impossibility of bonding four diortho-substituted aryl radicals to an atom of tin.

2. We have shown the possibility of synthesizing organotin compounds containing three diortho-substituted aryl radicals in which small molecular groups (CH_3, CH_3O, C_2H_5O) appear as substituents, and likewise three β-substituted naphthyl radicals. As is apparent from theoretical considerations, aryl radicals which do not contain ortho substituents, primary alkyl radicals (even those with a large and long side chain) and secondary alkyl groups may occur in these compounds as fourth radicals. The fourth valence may also be occupied by halogen.

3. We have given theoretical and experimental data on the true arrangement of three mesityl radicals linked to an atom of tin in the presence of a fourth non-mesityl radical.

4. Fourteen organotin compounds, not previously described in the literature, have been synthesized.

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THE SYNTHESIS OF LOW MOLECULAR WEIGHT POLYORGANOETHOXYSILOXANES OF REGULAR STRUCTURE

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The synthesis of polyorganosiloxanes by means of the hydrolysis or co-hydrolysis of various silicoorganic monomers gives polymers in which the distribution of monomers in the polymerized molecule has not been determined. It would be of interest to work out methods of synthesis which would guarantee the formation of polyorganosiloxanes with fixed or regular locations of the molecules in the chain. At the present time there are no methods which permit us to achieve the synthesis of polyorganosiloxanes with such a structure.

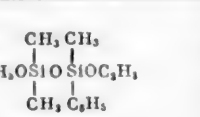
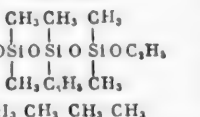
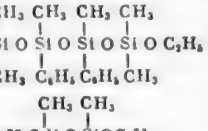
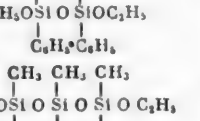
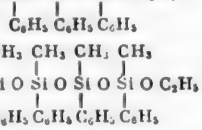
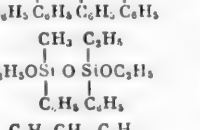
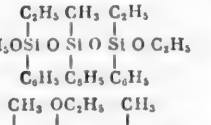
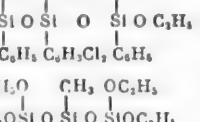
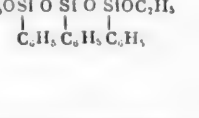
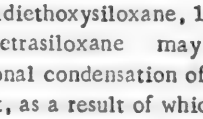
The present work is an effort to approach a solution to this problem. A synthesis of polyorganosiloxanes was outlined, whose polymeric chains would be constructed of atoms of silicon and oxygen with various organic groups alternating in given order about the silicon atom. It was proposed to accomplish this by synthesizing low molecular weight organosiloxanes containing alkoxy groups at the ends of the molecular chain, with the given organic radicals about the silicon atom. It was proposed to convert these compounds into polymers by heterofunctional condensations or other methods.

The synthesis and separation of products containing from two to four silicon atoms in the molecule and various organic groups will be examined below. The synthesis of these compounds was accomplished by heterofunctional condensation reactions [1-4] which for a given case may be represented by the following equation.

$$R_2SiCl_2 + 2R'_2Si(OR'')_2 \longrightarrow R''O\underset{\underset{R'}{|}}{\overset{\overset{R'}{|}}{Si}}O\underset{\underset{R}{|}}{\overset{\overset{R}{|}}{Si}}O\underset{\underset{R'}{|}}{\overset{\overset{R'}{|}}{Si}}OR'' + 2R''Cl$$

By the aid of this reaction methylphenyldichlorosilane was condensed with dimethyldiethoxysilane, with methylphenyldiethoxysilane, with ethylphenylethoxysilane, and with phenyltriethoxysilane. Methylphenyldiethoxysilane was also condensed with methylphenylchloroethoxysilane and with dichlorophenyldichloroethoxysilane. In all cases there was present in the reaction an excess of alkoxy producers in an amount sufficient to give compounds with functional ethoxy groups.

In studying the heterofunctional condensation of the compounds mentioned above, the reaction was 60-70% efficient as judged by the quantity of ethyl chloride given off. However, the separation of individual products presented greater difficulties and therefore their yield did not exceed 47%, and in some cases was only 13%. On separating the synthesized compounds by vacuum distillation the still residues always contained non-distillable products of high molecular weight. The properties of the compounds synthesized, separated and characterized in these experiments are shown in the table.

Name	Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}
1,1,3-Trimethyl-3-phenyl-diethoxydisiloxane		90—92° (1.5)	1.4432	0.9576
Pentamethyl-3-phenyl-1,5-diethoxytrisiloxane		107—110 (1)	1.4484	0.9850
Hexamethyl-3,5-diphenyl-1,7-diethoxytetrasiloxane		145—148 (1)	1.4660	1.0081
1,3-Dimethyl-1,3-diphenyldiethoxydisiloxane		119—120 (0.02)	1.4931	1.0251
1,3,5-Trimethyl-1,3,5-triphenyldiethoxytrisiloxane		153—156 (0.15)	1.5020	1.0535
1,3,5,7-Tetramethyl-tetraphenyl-1,7-diethoxytetrasiloxane		202—205 (0.02)	1.5101	1.0902
1-Methyl-3-ethyl-1,3-diphenyldiethoxydisiloxane		158—160 (1)	1.5020	1.0500
3-Methyl-1,5-diethyl-triphenyl-1,5-diethoxytrisiloxane		179—182 (1)	1.5113	1.0614
1,5-Dimethyl-1,5-diphenyl-3-ethoxy-3-dichlorophenyldiethoxytrisiloxane		92 (0.008)	1.5286	1.2137
1,5-Diethoxy-3-methyl-1,3,5-triphenyl-diethoxytrisiloxane		147—150 (0.008)	1.5012	1.0949

The formation of 1,1,3-trimethyl-3-phenyldiethoxysiloxane, 1-methyl-3-ethyl-1,3-diphenyldiethoxydisiloxane, and also hexamethyl-3,5-diphenyl-1,7-diethoxytetrasiloxane may be explained by the regrouping of functional groups. In order to confirm this the heterofunctional condensation of trimethylethoxysilane with methylphenyldichlorosilane in a molar ratio of 6:1 was carried out, as a result of which trimethylchlorosilane and methylphenyldiethoxysilane were separated out. Consequently the reaction went as follows

$$6(CH_3)_3SiOC_2H_5 + CH_3C_6H_5SiCl_2 \xrightarrow{FeCl_3}$$

$$\rightarrow 2(CH_3)_3SiCl + CH_3C_6H_5Si(OC_2H_5)_2 + 4(CH_3)_3Si(OC_2H_5).$$

The production of 1,1,3-trimethyl-3-phenyldiethoxydisiloxane is explained by the formation of methylphenylethoxychlorosilane in the first stage of the reaction.

$$(CH_3)_2Si(OC_2H_5)_2 + CH_3C_6H_5SiCl_2 \xrightarrow{FeCl_3}$$

$$CH_3C_6H_5Si(OC_2H_5)Cl + (CH_3)_2Si(OC_2H_5)Cl$$

Methylphenylethoxychlorosilane further enters into the reaction by condensation with a second molecule of dimethyldiethoxysilane (present in great excess).

$$CH_3C_6H_5Si(OC_2H_5)Cl + (CH_3)_2Si(OC_2H_5)_2 \xrightarrow{FeCl_3} CH_3C_6H_5SiOSi(CH_3)_2 + C_2H_5Cl$$
$$\quad\quad\quad

1,3,5-Trimethyl-1,3,5-triphenyldiethoxytrisiloxane was obtained from 47.7 g of methylphenyldichlorosilane, 210 g of methylphenyldiethoxysilane and 0.13 g of $FeCl_3$ by heating for six hours at 135-160°. Yield 42%.

Found %: Si 17.60; OC_2H_5 18.36. MR_D 135.6. $C_{25}H_{34}O_4Si_3$. Calculated %: Si 17.42; OC_2H_5 18.67. MR_D 138.5.

1,3,5,7-Tetramethyltetraphenyl-1,7-diethoxytetrasiloxane was isolated from the preceding experiment. Yield 17%.

Found %: Si 18.31; OC_2H_5 15.30. MR_D 169.5. $C_{32}H_{42}O_5Si_4$. Calculated %: Si 18.12; OC_2H_5 14.56. MR_D 169.3.

1-Methyl-3-ethyl-1,3-diphenyldiethoxydisiloxane was obtained from 95.5 g of methylphenyldichlorosilane, 448 g of ethylphenylethoxysilane and 0.54 g of $FeCl_3$ by heating for four hours at 103-104°. Yield 13%.

Found %: Si 14.81, OC_2H_5 25.02. M 352, MR_D 101.15. $C_{19}H_{28}O_3Si_2$. Calculated %: Si 15.55, OC_2H_5 25.0. M 360, MR_D 104.67.

3-Methyl-1,5-diethyltriphenyl-1,5-diethoxytrisiloxane was obtained from 95.5 g of methylphenyldichlorosilane, 448 g of ethylphenyldiethoxysilane and 0.54 g of $FeCl_3$ by heating for four hours at 102-104°. Yield 35%.

Found %: Si 16.3; OC_2H_5 18.87. Mol. wt. 528, MR_D 146.70. $C_{27}H_{38}O_4Si_3$. Calculated %: Si 16.47; OC_2H_5 17.64. Mol. wt. 510, MR_D 148.15.

1,5-Dimethyl-1,5-diphenyl-3-ethoxy-3-dichlorophenyldiethoxytrisiloxane was obtained from 58 g of dichlorophenyldichloroethoxysilane and 126 g of methylphenyldiethoxysilane in the presence of 0.09 g of $FeCl_3$ by heating for four hours at 122-150°. Yield 35%.

Found %: Si 15.04. Mol. wt. 595, MR_D 143.6. $C_{26}H_{34}O_5Si_3Cl_2$. Calculated %: Si 14.48. Mol. wt. 580, MR_D 141.9.

1,5-Diethoxy-3-methyl-1,3,5-triphenyldiethoxytrisiloxane was obtained from 19.1 g of methylphenyldichlorosilane and 72 g of phenyltriethoxysilane in the presence of 0.09 g of $FeCl_3$ by heating for four hours at 130-15[illegible]°. Yield 29%.

Found %: Si 15.96; OC_2H_5 36.35. Mol. wt. 580, MR_D 145.9. $C_{27}H_{38}O_6Si_3$. Calculated %: Si 15.49, OC_2H_5 33.2. Mol. wt. 542. MR_D 147.7.

SUMMARY

1. α, ω-ethoxyalkylarylsiloxanes of linear structure and containing 2-4 atoms of silicon in the molecule have been synthesized.

2. 1,5-Dimethyl-1,5-diphenyl-3-ethoxy-3-dichlorophenyldiethoxytrisiloxane and 1,5-diethoxy-3-methyl-1,3,5-triphenyldiethoxytrisiloxane were obtained.

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• Original Russian pagination. See C. B. Translation.

COMPLEX ORGANOSILICON ESTERS OF ACRYLIC AND METHACRYLIC ACIDS

I. SYNTHESIS OF MONOMERS

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Organosilicon derivatives of acids of the acrylic series, containing the $\geqslant SiOCOC(R) = CH_2$ grouping, have only been described in patents. In one of them [1] complex organosilicon esters of unsaturated acids of the general formula $(RCH = CR'COO)_xM(R'')_y$ are described. In this case R and R' are atoms of hydrogen or hydrocarbon radicals R" are halogen atoms, and M are atoms of silicon, tin or some other tetravalent element. In another patent [2], it is pointed out that by the interaction of tetraethoxysilane with methacrylic acid, triethoxysilylmethacrylate is obtained which is capable of being polymerized in the presence of benzoyl peroxide, and also of forming copolymers with various unsaturated organic compounds (styrenes, acids of the acrylic series, vinyl esters, etc.). Recently the synthesis and polymerization of complex organosilicon esters – derivatives of methacrylic acid containing the $\geqslant SiCH_2OCOC(R) = CH_2$ grouping have been described [3-5].

Previously we had described complex organosilicon esters of propionic and isobutyric acids, which were obtained by the interaction of the sodium salts of these acids with alkylchlorosilanes. In this way we obtained their unsaturated analogs: complex organosilicon esters of acrylic and methacrylic acids [6]

$$R_{4-x}SiCl_x + xMOCOC(R') = CH_2 \rightarrow R_{4-x}Si[OCOC(R') = CH_2]_x + xMCl,$$

where: R = CH_3 or C_2H_5; R' = H or CH_3; M is an alkali or alkaline earth metal.

The ionic character of the Si-Cl bond makes it possible to carry out this reaction in ordinary nonpolar solvents (benzene, petroleum ether, etc.) and to obtain complex esters with yields of 30-70%. In carrying out the analogous reaction with organosilicon compounds containing an atom of halogen in the α-position, it is necessary to conduct the reaction either under pressure at 180° [5], or in the presence of a strongly polar solvent (dimethylformamide) to which is added the corresponding free unsaturated acid [3].

All the complex esters obtained slowly polymerize on heating, and therefore in carrying on the synthesis it is necessary to introduce polymerization inhibitors (hydroquinone, picric acid, etc.) into the reaction mixture. Monomers that contain triacrylic or methacrylic radicals in the molecule show a particularly great tendency to autopolymerization. These compounds, which are low-melting crystalline substances, could not be obtained in pure form by fractionation in vacuo. They were separated out by freezing at low temperatures.

Simultaneously with the method of synthesis described above, a second method of obtaining these esters was examined. It is based on the reaction of alkylchlorosilanes with acrylic and methacrylic acids.

$$R_{4-x}SiCl_x + xHOOCC(R') = CH_2 \rightarrow R_{4-x}Si[OCOC(R') = CH_2]_x + xHCl.$$

Name of the ester	Formula	Boiling point (pressure in mm)	Melting point	d_4^{20}	n_D^{20}
Trimethylsilylacrylate	$(CH_3)_3SiOOCCH=CH_2$	53—54° (62)	—	0.8939	1.4112
Triethylsilylacrylate	$(C_2H_5)_3SiOOCCH=CH_2$	77—78 (14)	—	0.9014	1.4332
Dimethylsilyldiacrylate	$(CH_3)_2Si(OOCCH=CH_2)_2$	86—91 (10)	—	1.0475	1.4340
Diethylsilyldiacrylate	$(C_2H_5)_2Si(OOCCH=CH_2)_2$	113—114 (13)	—	0.9951	1.4353
Methylsilyltriacrylate	$CH_3Si(OOCCH=CH_2)_3$	—	15—18°	—	—
Ethylsilyltriacrylate	$C_2H_5Si(OOCCH=CH_2)_3$	—	21	—	—
Trimethylsilylmethacrylate	$(CH_3)_3SiOOCC(CH_3)=CH_2$	51—51.5 (20)	—	0.8898	1.4131
Triethylsilylmethacrylate	$(C_2H_5)_3SiOOCC(CH_3)=CH_2$	65—65.5 (6)	—	0.9058	1.4390
Dimethylsilyldimethacrylate	$(CH_3)_2Si[OOCC(CH_3)=CH_2]_2$	96—98 (7)	25—26	1.0070	1.4390
Diethylsilyldimethacrylate	$(C_2H_5)_2Si[OOCC(CH_3)=CH_2]_2$	125—128 (19)	—	0.9907	1.4430
Methylsilyltrimethacrylate	$CH_3Si[OOCC(CH_3)=CH_2]_3$	—	34—36	—	—
Ethylsilyltrimethacrylate	$C_2H_5Si[OOCC(CH_3)=CH_2]_3$	—	16—18	—	1.4303

However, the yields of monomers in this case are significantly lower than in the first method.

These complex esters are either colorless, clear liquids or crystalline substances with low melting points. They are all easily hydrolyzed by water. The tendency to hydrolysis increases with an increasing number of of acyloxy groups in the molecule. Esters that contain one acyloxy group have a camphor-like odor. Esters with two or three acyloxy groups have the usual odor of the corresponding unsaturated acids, which is due to the slight hydrolysis of these esters by the moisture in the air. Data on the twelve complex esters that were synthesized are presented in the table.

Comparison of the constants of the complex monomeric esters of the corresponding saturated [6] or unsaturated acids permits one to conclude that the introduction of a double bond into the aicd radical causes a significant increase in the specific gravity and the index of refraction of the esters, but it has little effect on the boiling point. The general laws for the change of the constants of these esters when ethyl groups are substituted in place of methyl radicals have been published previously [6].

EXPERIMENTAL SECTION

The synthesis of complex organosilicon esters of acrylic and methacrylic acids was carried out by a previously described method [6]. The dry salt of the unsaturated acid, a dry solvent (benzene or petroleum ether) (200-250 ml per g mole of salt) and 0.5-1.0 g of inhibitor (hydroquinone or picric acid) were introduced into a flask equipped with a mercury seal, a mechanical stirrer, a dropping funnel and a reflux condenser attached to a Tishchenko flask containing concentrated H_2SO_4. Alkylchlorosilane was added (0.5-0.6 g-mole per mole of salt) through the dropping funnel and the mixture stirred. The flow was adjusted so as not to cause vigorous heating of the mixture. The reaction was completed by stirring the reaction mixture at room temperature for from 20-40 hours. The solution was separated from the solid salt by rapid filtration through a porous glass filter. A small quantity (0.5-1.0 g) of inhibitor was added to the filtrate, the solvent was evaporated at room temperature under the vacuum of a water pump, and the remainder was fractionated in vacuo.

The complex esters containing three acyloxy groups were separated out by freezing at -50 to -80° and filtration of the crystalline substances at the same temperatures. In carrying out all these operations it is essential to avoid prolonged contact of the materials with moist air. The yields of monomeric esters varied from 30 to 70%.

The determination of silicon was accomplished by the mineralization of a batch of the polymer (obtained from the monomer) by a mixture of concentrated H_2SO_4 and HNO_3. The molecular weights of the monomers were determined by the cryoscopic method in benzene; the esterification numbers were obtained by the saponification of the monomers by a solution of caustic potash in diethyleneglycol.

Yield, %	MR_D		M		Esterification no.		% Si	
	found	calc.	found	calc.	found	calc.	found	calc.
44.2	40.07	39.83	135, 138	144.22	393, 397	389	19.11, 19.57	19.44
28.2	53.73	53.72	184, 185	186.29	294, 296	301	15.15, 15.09	15.06
37.2	49.75	49.38	204, 206	200.24	557, 557	560	13.20, 13.33	14.01
45.3	59.90	58.64	222, 224	228.29	487, 489	491	12.21, 12.16	12.29
28.1	—	—	—	256.26	648, 643	656	11.12, 11.41	10.94
30.4	—	—	—	270.28	601	622	10.69, 11.02	10.38
58.2	44.34	44.46	162, 183	158.24	352, 350	354	17.08, 16.96	17.73
54.9	58.16	58.35	210, 215	200.32	284, 287	280	13.95, 13.78	14.01
67.4	58.74	58.64	210, 239	228.29	493, 494	491	12.11, 12.18	12.29
27.9	68.58	67.90	257, 258	256.34	435, 435	437	10.97, 11.02	10.94
32.4	—	—	316	298.33	569, 572	564	9.04, 8.91	9.39
37.1	—	—	307	312.34	536, 538	538	8.78, 8.96	8.98

SUMMARY

From the reaction of salts of acrylic and methacrylic acids with methyl- and ethylchlorosilanes, 12 complex organosilicon esters, not previously described in the literature, were obtained. It has been determined that these esters are capable of polymerization.

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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Metrology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.